

- VOLUME C -

IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

PHARMACYCLICS LLC and : CIVIL ACTION
JANSSEN BIOTECH, INC., :

Plaintiffs, :

vs. :

CIPLA LIMIGTED, et al., :

Defendants. : NO. 18-192 (CFC)

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PHARMACYCLICS LLC and : CIVIL ACTION
JANSSEN BIOTECH, INC., :

Plaintiffs, :

vs. :

ALVOGEN PINE BROOK LLC and :
NATCO PHARMA, :

Defendants. : NO. 18-275 (CFC)

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Wilmington, Delaware
Thursday, October 15, 2020
8:30 o'clock, a.m.

- - -

BEFORE: HONORABLE COLM F. CONNOLLY, U.S.D.C.J.

- - -

Valerie J. Gunning
Official Court Reporter

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P R O C E E D I N G S

(Proceedings commenced in the courtroom
beginning at 8:30 a.m.)

THE COURT: All right. Good morning. Are you
all there? Good morning, all. Are you all there?

MS. BHARKHDA: Yes, Your Honor.

MS. CLAYTON: Good morning, Your Honor.

THE COURT: Ms. Clayton, anything we need to
address before we start testimony today?

MS. CLAYTON: No. We're still discussing with
Alvogen about the time. We hope to come to an agreement.
If not, we can let you know.

THE COURT: Let's make sure we tackle that. If
it's not resolved at the mid-morning break, we'll tackle it
right after. All right?

MS. CLAYTON: Good morning, Your Honor. Thank
you.

THE COURT: Ms. Bharkhda, anything from you from
the plaintiffs' side?

MS. BHARKHDA: I would be happy to address the
question you posed to us at the end of the day yesterday
regarding confidential information if Your Honor would like
to hear about that. If we are going to do it, I would

1 suggest we do it outside the presence of Dr. Swift, but I'm
2 happy to address it if you would like.

3 THE COURT: Is it going to come up in her
4 testimony? Was it her testimony or the prior testimony?

5 MS. BHARKHDA: It was.

6 THE COURT: So let's quickly address it. We'll
7 put Dr. Swift in a waiting room real briefly and address it.
8 All right?

9 Dr. Swift, good morning.

10 MS. BHARKHDA: Yes, Your Honor. So I think Your
11 Honor is correct, that one could potentially consult
12 confidential documents in order to confirm the presence of
13 an inherent property that would result from, necessarily
14 result from a disclosed invention or product. However, that
15 is, and we took a look at with an I believe was the opinion
16 you were referring to and I think that's a very different
17 situation than what we have here.

18 Alvogen is not making an argument that the
19 confidential documents are confirming an inherent property
20 of ibrutinib. What they are saying is they show that what
21 was used in the Phase 1 study was crystalline form A in the
22 doses that were given to the patient.

23 Now, the fact that it's crystalline form A is
24 not an inherent property of ibrutinib. As you have heard
25 quite a bit I think earlier in the case, there are multiple

1 forms of crystalline ibrutinib. There's amorphous
2 ibrutinib. So the choice of which one of those went into
3 the dosages is not an inherent property and so we don't
4 think that the use of confidential information to the extent
5 that it is permissible, we're showing an inherent property
6 or limitation is present in a reference that discloses some
7 particular disclosure about the art applies here at all.

8 THE COURT: So I had thought they were going to
9 show essentially that form A was used and the data showed it
10 was 2-Theta. There were 2-Theta peaks rather.

11 MS. BHARKHDA: Correct. But it goes further
12 than that because my understanding of Alvogen's argument is
13 by virtue of using the code name, PCI-32765, that would tell
14 a POSA in and of itself not only that you were using
15 ibrutinib, but that that code name itself, PCI-32765, is
16 necessarily and only and always associated with form A of,
17 crystalline form A of ibrutinib and then taking it a step
18 further, that form A has those peaks.

19 So it's not just to prove the XRPD limitation.
20 It is to prove that crystalline form A was actually used in
21 the studies even though there are other options and that is
22 not the type of scenario that confidential information could
23 be used for.

24 THE COURT: Okay. But now let me ask you.
25 Before I even hear from Mr. Gutman, let's just assume what

1 you are saying is uncontested. Then why don't you just save
2 it and on cross-examination, you just ask the witness, by
3 the way, ibrutinib comes in other forms.

4 MS. BHARKHDA: Your Honor, we plan to have that
5 discussion with Dr. Swift, absolutely. We are going to have
6 that. I think Your Honor asked a question about what the
7 confidential information was going to be used for and
8 whether or not that was an appropriate use of confidential
9 information, in the inherent anticipation context.

10 We can certainly elicit testimony from Dr. Swift
11 about what she's using that information for. That's my
12 understanding.

13 THE COURT: Okay.

14 MS. BHARKHDA: And so I don't think that is a
15 proper use of confidential information in this scenario.

16 THE COURT: All right. I am going to let it in.
17 If you are right, it will be, you know, addressed probably
18 pretty adequately on cross and maybe Mr. Gutman is going to
19 show that you're not right, and he can do that through the
20 testimony.

21 So I'm going to overrule the objection and let
22 the witness discuss it. Okay? All right. Thank you.

23 MS. BHARKHDA: Thank you, Judge.

24 THE COURT: All right. Thank you.

25 Mr. Gutman, are you ready?

Swift - direct

1 MR. GUTMAN: Yes Your Honor.

2 THE COURT: All right. We can bring the witness
3 back in and continue.

4 ... DR. JENNIFER ANN SWIFT, having been
5 previously duly sworn/affirmed as a witness, was examined
6 and testified further as follows ...

7 DIRECT EXAMINATION, Continued.

8 BY MR. GUTMAN:

9 Q. Good morning, Swift.

10 A. Good morning.

11 Q. I believe yesterday we left off where you were
12 discussing DTX-1514 and what that was. I think we had slide
13 17 up. And can you describe what slide 17 is?

14 A. Yes. This is an excerpt from the clinical study
15 report, PCY-04753, which was the Phase 1 dose escalation
16 study that we talked about yesterday and this particular
17 excerpt identifies the lot numbers of ibrutinib that were
18 used in that clinical study. Those numbers are all
19 highlighted and underlined in red.

20 Q. And in the upper right-hand corner, there's a
21 reference to clinical study report PYC-04753.

22 Do you see that?

23 A. Yes.

24 Q. What's your understanding about what that was
25 referring to?

Swift - direct

1 A. So that is the specific code referring to the clinical
2 study that was done, that was reported by Pollyea.

3 Q. And is that a Phase 1 dose escalation study?

4 A. Yes.

5 Q. Are you aware of -- how many Phase 1 dose escalation
6 studies are you aware of that were conducted on PCI-32765?

7 A. I am only aware of one. If there are more than one,
8 it would have a different clinical study report number, but
9 I am only aware of one.

10 Q. Can we go to slide 18, please. Now, can you please
11 describe what is here on this slide?

12 A. Yes. So this is from the IND report and there are two
13 columns of numbers that are highlighted. The ones in the
14 middle of the page correspond to the lot number, the drug
15 product number, and those are the same numbers that are in
16 the previous slide from the PCYC study.

17 What this table does, it correlates the drug
18 product batch or lot number with the drug substance number.
19 That's the column on the left-hand side.

20 Q. Now, if you could go to slide -- so actually, before
21 me move on, so what's your understanding about whether the
22 batch numbers or the drug substance that are identified in
23 the left-hand-most column, how those relate to the batch
24 numbers for the PCI-32765 drug product that were used in the
25 Phase 1 dose escalation study?

Swift - direct

1 A. The way to line up the numbers, that's what I'm trying
2 to do here. In the previous slide I have the drug product
3 number. What this table does, it matches up each and every
4 one of the lot numbers in the clinical study with the batch
5 numbers that were used in that study.

6 Q. Can we go to slide 19, please.

7 Now, can you please tell us what is on this
8 slide?

9 A. Yes. And this is the table that follows the previous
10 table that I just showed where it takes those batch numbers
11 for the drug product and these are underlined again, and it
12 gives additional information, such as who manufactured that
13 material, the manufacturing date as well as the crystalline
14 form that is present in those samples. And what you will
15 notice is that in every single column, which is highlighted,
16 it indicates that the crystalline form that was used in
17 those clinical studies was form A, the form A of PCI-32765,
18 which we know as ibrutinib.

19 Q. So based on this information regarding the batches
20 that were used in the Phase 1 dose escalation study for
21 PCI-32765, have you developed any opinions about what
22 crystalline form PCI-32765 was in when it was used in that
23 Phase 1 dose escalation study?

24 A. It says quite clearly that it was form A,
25 unambiguously. There's no other option but for it to have

Swift - direct

1 been form A in those dose escalation studies.

2 Q. Do you have an opinion about whether PCI-32765 as used
3 in the Phase 1 dose escalation study disclosed in Pollyea
4 2009 is necessarily referring to crystalline form A of
5 ibrutinib?

6 A. Yes. Absolutely.

7 Q. Can we go to slide 20, please. Can you please
8 describe what this slide is?

9 A. So this slide identifies the compound in question with
10 its product name, ibrutinib. Identifies it with the
11 PCI-32765. These terms are being used synonymously. It
12 gives the chemical name and it also gives you the chemical
13 structure. It draws out the molecule for you.

14 Q. Can we go to DTX-1646, please. Dr. Swift, what is
15 DTX-1646?

16 A. This is a powder X-ray analysis that was performed by
17 a private company on different lot numbers of PCI-32765 on
18 behalf of Pharmacyclics.

19 Q. Can you please go to slide 23. Can you please
20 describe what's on slide 23?

21 A. So slide 23 has a comparison between one of the lot
22 numbers, 111365, which is, I believe, one of the lot numbers
23 that was used in the dose escalation study, and it compares
24 it against a reference standard, which is lot 11003. And
25 it's comparing those two powder X-ray patterns.

Swift - direct

1 Q. And what does this tell you about whether lot 111365
2 of PCI-32765 that was used in the Phase 1 dose escalation
3 study is crystalline form A of ibrutinib as recited in claim
4 5 of the '455 patent?

5 A. Well, the lot 11003 is identified in this lot as form
6 A. It makes sense that's the reference standard. And when
7 you compare it up against the powder pattern for this lot
8 111365, the two powder patterns have peaks in all the same
9 spots so that you would conclude that this actually is a
10 good match. Almost an ideal match for form A.

11 Q. Does this confirm your previous conclusions based on
12 the batch records that lot 111365 is crystalline form A as
13 recited in claim 5 of the '455 patent?

14 A. Yes. So the IND report refers to it as form A. When
15 you actually look the raw data, the raw data also confirms
16 that it's form A.

17 Q. Now, were there other lots of PCI-32765 that were used
18 in the Phase 1 dose escalation study disclosed in Pollyea
19 2009 that were addressed in this report, that is DTX-1646?

20 A. Yes. This report compares several lot numbers and
21 each and every one of them corresponds to form A.

22 Q. Now, just briefly, based on your conclusion that all
23 of the lots used in the Phase 1 dose escalation study are
24 crystalline form A of ibrutinib, can you explain why those
25 lots would also have the 2-Theta peak positions that are

Swift - direct

1 recited in claim 5 of the '455 patent?

2 A. The six lines of -- the six powder diffraction lines
3 that are cited in the '455 patent are present in those
4 samples. The X-ray pattern that form A gives as an inherent
5 property of that form is associated with the powder pattern
6 with the form because you can't make the powder pattern
7 without the form.

8 Q. Have you seen evidence that demonstrates that
9 PCI-32765 as used in the Phase 1 dose escalation study
10 necessarily refers to crystalline form A of ibrutinib with
11 the 2-Theta peaks recited in claim 5 of the '455 patent?

12 A. Yes. I checked every single powder pattern
13 corresponding to every single lot and in every single powder
14 pattern, it has the six powder diffraction patterns that are
15 cited in the '455 patent.

16 Q. Can you turn to DTX-0148, please. Dr. Swift, what is
17 DTX-0148?

18 A. This is the article entitled BTK inhibitor, PCI-32765,
19 induces durable responses with minimal toxicity in patients
20 with relapsed/refractory B cell malignancies: Results from
21 a Phase 1 study. The first author is Nathan Fowler and it
22 was published in the journal Blood.

23 Q. And is this prior art to the '455 patent?

24 A. Yes, it is.

25 Q. Do you have an opinion about whether Fowler 2010,

Swift - direct

1 which is DTX-0148, anticipates claim 5 of the '455
2 patent?

3 A. Yes, I think it does anticipate the claim. This is an
4 update on the Phase 1 dose escalation study. So for all the
5 same reasons that I think Pollyea anticipates the claims of
6 the patent at issue, I think this one does as well.

7 Q. Can we go to DTX-1700, please. Dr. Swift, what is
8 DTX-1700?

9 A. DTX-1700 is a journal article by Vit Zvonicek, I'm not
10 sure how to pronounce his name as the first author that was
11 published in crystalline growth and design. The paper
12 discusses ibrutinib polymorphs.

13 Q. Can we go to slide 24, please. And what did DTX-1700
14 disclose with respect to the crystalline form A of
15 ibrutinib?

16 A. So they identified form A as the most stable polymorph
17 on the basis of its melting point compared to other forms.
18 And they also state quite clearly that the preparation of
19 form A did not present any challenges because it was the
20 most thermodynamically stable polymorph. It was obtained as
21 a solid for most of the screening experiment.

22 Q. Would that be consistent with the fact that
23 crystalline form A is the most stable polymorph of
24 ibrutinib?

25 A. Yes. That's exactly what they say.

Swift - direct

1 Q. Can we go to JTX-0551, please. Can you please
2 describe what JTX-0551 is.

3 A. So this is a study conducted by a company on the
4 market. The title is called polymorphism studies on PCI
5 32765-00 for Pharmacyclics.

6 Q. And can you go to the next page, please. Do you see
7 at the top there's a reference to customer details?

8 A. Yes.

9 Q. What is the name of that customer?

10 A. So the customer is Pharmacyclics with a contact person
11 as Dr. Mark Swift.

12 Q. Do you have an understanding about whether Dr. Swift
13 is a named inventor on the '455 patent?

14 A. I believe he is.

15 Q. Can we go to slide 44, please. Dr. Swift, what were
16 the conclusions that were drawn from the polymorphism study
17 that was addressed in JTX-0551?

18 A. So some of the major conclusions are highlighted on
19 this slide here. They report that the fact that form A is
20 easy to produce and control was a significant advantage over
21 other forms both because it was easy to get and because you
22 could competently make it over and over and over again. The
23 fact that it's a thermodynamically stable form means that
24 you also don't have to worry about it converting to
25 something else because it's already a thermodynamic bottom.

Swift - direct

1 And, you know, from that, the last sentence here
2 is that they actually recommended it as the ideal
3 crystalline form to move forward in development steps
4 because -- precisely for those reasons.

5 Q. Can we go to DTX-1683, please. Can you identify what
6 is DTX-1683?

7 MS. BHARKHDA: Your Honor, sorry. We have an
8 objection to DTX-1683.

9 THE COURT: Okay.

10 MS. BHARKHDA: This was a portion, excerpted
11 portion of prosecution history documents from the
12 prosecution of something other than the '455 patent. It
13 postdates the patent and it doesn't discuss either the
14 Pollyea or Fowler references.

15 THE COURT: So is the objection on relevance?

16 MS. BHARKHDA: The objection is on relevance,
17 hearsay. There doesn't seem to be any connection between
18 this and the '455, the actual claims of the '455 patent.
19 It's addressing the prosecution of a different later patent.

20 THE COURT: All right.

21 MS. BHARKHDA: It doesn't discuss any of the
22 references.

23 THE COURT: It's a relevance and hearsay
24 objection. All right. Mr. Gutman, it is hearsay. Right?

25 MR. GUTMAN: No, it's not, Your Honor. We're

Swift - direct

1 going to be using this to demonstrate that the ibrutinib
2 with various peaks -- first of all, let me start out by
3 saying, this is a related application to the '455 patent.

4 THE COURT: Wait. I mean, I'm sorry. Just
5 address the hearsay objection. I thought you were going to
6 say, sure, it's hearsay, but there's an objection. Isn't it
7 hearsay?

8 MR. GUTMAN: No, it's not hearsay, because we're
9 not offering it for the truth of the matter asserted, Your
10 Honor.

11 THE COURT: Okay. You're not going to offer
12 then anything in this document for the truth of the matter
13 asserted. Really? I'm going to be surprised at that. I
14 mean, you are not going to say -- maybe. Okay. Why is it
15 relevant? Let's go to the relevance then.

16 MR. GUTMAN: Yes. It's relevant because claims
17 that are similar to the claims that are being asserted in
18 claim 5 of the '455 patent were considered in a related
19 application within the same family. The claims that are
20 similar that cover ibrutinib were rejected by the Patent
21 Office for various reasons that are consistent with the
22 testimony that you have heard today and the applicant didn't
23 respond to the office action which rejected these claims and
24 abandoned the claims.

25 So that's highly relevant because it shows, it

Swift - direct

1 shows what plaintiffs' thinking was with respect to the
2 validity of the claim that is being asserted against
3 Alvogen.

4 THE COURT: Okay.

5 MS. BHARKHDA: Your Honor, may I respond?

6 THE COURT: No, because I've got to try to
7 understand what Mr. Gutman just said.

8 So this is a -- this is an amendment proposed by
9 Pharmacyclics? Mr. Gutman?

10 MR. GUTMAN: Yes.

11 THE COURT: So it's an amendment proposed by
12 Pharmacyclics in 2018. It's an amendment proposed to a
13 patent application that is not, it's clearly not the patent
14 at issue here.

15 You are saying though it's a similar patent with
16 similar claims to the patent, and you are saying that
17 Pharmacyclics' failure to respond, or not failure, but the
18 fact that it didn't respond to the rejection of these
19 proposed amendments is probative?

20 MR. GUTMAN: Not just that it didn't respond,
21 but it allowed the application to be abandoned, and I think,
22 Your Honor, even if this was hearsay, I think it falls under
23 a hearsay exception. It's a statement against party
24 interest and it's a public record.

25 THE COURT: What is the statement against

Swift - direct

1 interest?

2 MR. GUTMAN: The statement against interest is
3 the fact that they didn't respond and they let the
4 application be abandoned.

5 THE COURT: I'm going to sustain the objection.
6 I don't see any relevance to this and I don't think it has
7 very probative value for sure.

8 I think it's unduly confusing and under 403, I a
9 ban it because frankly there has not been a proffer that
10 makes me persuaded that the probative value of this is
11 sufficient and I think the danger of confusion and prejudice
12 substantially outweighs any probative value it could
13 possibly have. All right. Sustained.

14 MR. GUTMAN: Can you please turn to DTX-0278.

15 BY MR. GUTMAN:

16 Q. Dr. Swift, before we address this document, do you
17 have an opinion about whether claim 5 of the '455 patent is
18 obvious?

19 A. I do. My conclusion based on what I have seen is that
20 it is obvious.

21 Q. What is DTX-0278?

22 A. This is a journal article from PNAS. The first author
23 is Lee Honigberg. The title is the Bruton Tyrosine Kinase
24 Inhibitor PCI-32765 blocks B cell activation and is
25 efficacious in models of autoimmune disease and B cell

Swift - direct

1 malignancy. It was published in July 2010.

2 Q. Can we go to slide 48, please.

3 Now, if I refer to DTX-0278 as Honigberg 2010,
4 would you understand what I'm referring to?

5 A. Yes.

6 Q. What does Honigberg 2010 disclose about PCI-32765?

7 A. So you can see in Figure 1, it discloses the chemical
8 structure. It draws the molecule out for you. It
9 identifies it as a BTK inhibitor.

10 Q. And can we go to slide 49, please.

11 What does Honigberg 2010 say about the clinical
12 activity of PCI-32765?

13 A. So it spells out for the reader that it's currently
14 undergoing human clinical development in patients and that
15 it has shown promising activity. It's potent, it's highly
16 selective, and it presents a potentially unique therapeutic
17 approach to treating various diseases.

18 Q. Now, based on what we've seen that Honigberg 2010
19 discloses, would a POSA prior to June 4, 2012, have been
20 motivated to make crystals of ibrutinib or PCI-32765?

21 A. I think they would have.

22 Q. Can you explain why?

23 A. So if you have a drug compound that shows promising
24 clinical activity, most patients would prefer to take some
25 oral tablet than be required to have an injectable. So you

Swift - direct

1 would be motivated to try to put that drug company into a
2 stable form that could be delivered in a, in a pill or a
3 tablet or capsule. In order to do that, you would need to
4 do polymorph screening and identify stable forms that could
5 be safely delivered to a patient.

6 Q. And did methods exist prior to June 4th, 2012, that
7 would have allowed a POSA to make crystals of ibrutinib or
8 PCI-32765?

9 A. Sure. The standard protocol for how you would go
10 about it, how you would at least start the polymorph
11 screening.

12 Q. Now, based on what Honigberg 2010 discloses, would a
13 POSA have been motivated prior to June 4th, 2012, to screen
14 for different polymorphs of ibrutinib or PCI-32765?

15 A. I would think so. As disclosed in the paragraph, if
16 it's undergoing human clinical development, I assume
17 somebody has already gone to the trouble of screening for
18 polymorphs, so a POSA would probably conclude that somebody
19 has already done it. If they hadn't already done it, they
20 needed to have done it or they would certainly be motivated
21 to do it.

22 Q. And were there methods available to a POSA prior to
23 June 4, 2012, that a POSA could have used to do polymorph
24 screening?

25 A. Sure. There are plenty of conventional methods on how

Swift - direct

1 you would approach screening of polymorphs.

2 Q. And based on the disclosures of Honigberg 2010, would
3 a POSA have been motivated to characterize any polymorphs
4 that resulted from the polymorph screening?

5 A. Yes. If you are going to make them, you are certainly
6 going to characterize them.

7 Q. And were there methods available prior to June 4th,
8 2012, that would have allowed a POSA to characterize any
9 polymorphs?

10 A. Yes. I think at the beginning of my testimony
11 yesterday, I answered a variety of very different
12 conventional methods that a POSA would use to characterize
13 polymorphic material. These include X-ray diffraction,
14 powder X-ray diffraction, thermal methods, spectroscopic
15 methods.

16 Q. Would a POSA reasonably, based on the disclosures of
17 Honigberg 2010, would a POSA have reasonably expected to
18 succeed at making a crystalline form A of ibrutinib as
19 recited in claim 5 of the '455 patent?

20 A. I believe that any POSA that would embark upon trying
21 to crystallize PCI-32765 would be able to get crystalline
22 materials. If you are starting a polymorph screen, you get
23 the most stable form early in the process. We know form A
24 is the most stable form and if you have form A and you take
25 a powder pattern of it, it's going to have the six

Swift - direct

1 refraction lines that are recited in claim 5 of the asserted
2 patent.

3 Q. Can we go to DTX-0001, please. Thank you.

4 Dr. Swift, what is DTX-0001?

5 A. This is a patent, 7,514,444, that was, it's entitled
6 inhibitors of Bruton's tyrosine kinase. It was issued on
7 April 7th, 2009.

8 Q. Is it prior art to the '455 patent?

9 A. Yes, it is.

10 Q. Does the '444 patent disclose ibrutinib?

11 A. Yes, it does.

12 Q. And would a POSA have been motivated to crystallize
13 ibrutinib pursuant to the teachings of the '444 patent?

14 A. Yes. So this patent, broadly speaking, discloses the
15 synthesis of several compounds, ibrutinib among them. And
16 in the text of the patent, it spells out very conventional
17 methods for how one would go about purifying their materials
18 and crystallizing them.

19 Q. Can we go to slide 33, please. Can you briefly
20 describe what the '444 patent says about the methods that
21 were available to crystalline ibrutinib?

22 A. So in the -- in any synthesis, if you are isolating a
23 solid, it's conventional to try to purify that material and
24 you would use conventional methods, including
25 crystallization and filtration among them. Once you have

Swift - direct

1 purified your materials, you would try to, you would
2 characterize it. Right? Every, every chemist would try to
3 make pure materials and then, you know, if you have gone to
4 the trouble of making it, you would most certainly
5 characterize it.

6 So once you have made it, again, you would --
7 you'd be using these conventional techniques,
8 crystallization and recrystallization among them.

9 Q. Can we go to slide 42 please. What is the '444 patent
10 describing here?

11 A. So the -- what's shown on the slide is the abstract.
12 The patent tells you how to make them and it tells you why
13 they're interested in making them and the reason why they
14 are interested in making them is because they have potential
15 for treating autoimmune diseases and other diseases, like
16 cancer.

17 Q. And is lymphoma mentioned as one of those diseases?

18 A. Yes. Lymphoma.

19 Q. And how does this disclosure fit in with your opinions
20 that a POSA would be motivated to make and obtain
21 crystalline form A of ibrutinib?

22 A. So if you, if you tell me how to make the compound and
23 you tell me I can use conventional methods to create
24 crystalline forms of that material and that that material
25 will have some therapeutic value in patients, I think that

Swift - direct

1 provides sufficient motivation to do so.

2 Q. Can we go to DTX-1688, please. What is DTX-1688, Dr.
3 Swift?

4 A. So this is a book chapter. This is just the cover of
5 the book. So the book is pharmaceutical sciences. It's
6 from 1990. The chapter I think you are asking about is
7 chapter 75 on pre-formulations.

8 The first author is Lewis Ravin.

9 Q. Can you briefly describe what is pre-formulation?

10 A. The pre-formulation are the early steps that one would
11 take in the development process to try to characterize the
12 physicochemical properties of the drug substance.

13 Q. Can you go to the Bates page ending in 113, the first
14 full paragraph on the right-hand column. Oh, I'm sorry.
15 And the second paragraph as well. Thank you.

16 Can you describe what DTX-1688 is saying here,
17 Dr. Swift?

18 A. So it's saying in very general terms that once you
19 establish that you can, that if polymorphism is an issue for
20 your compound, then you would be using a variety of
21 techniques to try to characterize that material. It's
22 important to identify different polymorphic forms and to
23 isolate them and to characterize them.

24 Q. Can we turn to the Bates page ending in 1114, and then
25 the first sentence in the left-hand column.

Swift - direct

1 And what is this -- the first full sentence,
2 what is DTX-1688 saying here, Dr. Swift?

3 A. So as I introduced yes, if there are multiple forms,
4 multiple polymorphs of a compound, only one gets the
5 thermodynamically most stable form. And what this statement
6 in this paper says is that the, metastable form, which is by
7 definition anything except the thermodynamic form, that it
8 has the potential to convert to other -- well, the statement
9 says that it will convert to the stable forms over time.

10 Q. And what -- what do you take away from that with
11 respect to crystalline form A of ibrutinib?

12 A. Well, I already know that form A from multiple sources
13 is the most stable, most thermodynamically stable form, so I
14 would expect that it does not convert to anything else.
15 Other forms would convert to form A, not the other way
16 around.

17 Q. Can we go to DTX-147, please. What is DTX-147?

18 A. So this is a document by the FDA, which provides
19 industry guidance on pharmaceutical quality for
20 manufacturing, manufacturing and control information.

21 Q. And when was this published?

22 A. July 2007.

23 Q. Can we go to slide 55, please? And what is DTX-147?
24 Does it recommend anything with respect to conducting a
25 polymorph screen?

Swift - direct

1 A. So FDA's main objective is to protect the public, and
2 part of that is to advise companies that if you were
3 delivering a drug and trying to do that in solid form, you
4 need to be aware of polymorphism and you need to screen for
5 it, because they say in the highlighted sentence here that
6 polymorphism can affect the quality, safety, and efficacy of
7 the drug product that's given to the public.

8 Q. Can we go to DTX-1025, please. Dr. Swift, can you
9 please tell us what is DTX-1025?

10 A. So 1025 is a book chapter. The picture that's being
11 shown is just the cover. The chapter that's cited is
12 chapter five, which is generation of polymorphs, hydrates,
13 solvates, and amorphous solids. It's authored by J. K.
14 Guillory. The publication came out in 1999.

15 Q. Can we go to slide 57, please.

16 Can you please tell us what is on this slide,
17 Dr. Swift, with respect to DTX-1025, the Guillory reference
18 and the '455 patent?

19 A. Yes. So in this slide, Table 1 is reproduced from
20 this reference. It's a shorter solvent table. I know I
21 gave you a very long table and this is a difference, a
22 solvent that one might use to prepare polymorphs and do a
23 polymorph screen. This is just a very much shortened
24 version of it.

25 And on the right-hand side is an excerpt from

Swift - direct

1 the '455 patent, which lists some of the solvents that form
2 A can be obtained from. And the purpose of juxtaposing
3 these two items next to one another is to draw attention to
4 the fact that the solvents that are being used to generate
5 form A are very much the same solvents that are cited in
6 most of the solvent tables.

7 Q. Dr. Swift, do you have an opinion, do you have an
8 opinion about what references render the obvious -- render
9 obviousness claim -- let me back up. Excuse me.

10 Do you have an opinion about what references
11 render obvious claim 5 of the '455 patent?

12 A. So as I said over the last two days, I think that
13 there are several references that make claim 5 obvious.
14 Honigberg 2010 tells you that there is a drug that has
15 potential to treat diseases. The '444 patent tells you that
16 you can -- tells you how to make that drug and that you
17 should use conventional methods to prepare it. References
18 that were introduced yesterday and introduced Miller 2007,
19 which was the, a list of solvents, a much longer list of
20 solvents than this one, which instructed you how to do a
21 polymorph screen as well as the Bauer reference from
22 yesterday, which was from 2008, which spoke about the
23 importance in a pharmaceutical context with trying to do a
24 polymorph screen.

25 I think the sum total of those four references

Swift - cross

1 alone speaks to the obviousness, but there are actually many
2 more references that one could cite and 20 of institutional
3 acquired knowledge that would also speak to the fact that
4 really anybody in their right mind would conduct a polymorph
5 screen knowing that you are going to try to put this in a
6 pharmaceutical product.

7 MR. GUTMAN: Thank you, Dr. Swift. I have no
8 further questions, Your Honor.

9 THE COURT: All right. Thank you.

10 Cross-examination.

11 CROSS-EXAMINATION

12 BY MS. BHARKHDA:

13 Q. Good morning, Dr. Swift.

14 A. Good morning.

15 Q. Prior to your involvement in this case, you had never
16 worked with ibrutinib; is that correct?

17 A. That's correct.

18 Q. And you were not aware of ibrutinib before you were
19 engaged by Alvogen to work on this case; correct?

20 A. I'm sorry. There was somebody playing something. If
21 you could just restate the question.

22 Q. You were not aware of ibrutinib before you were
23 engaged by Alvogen to work on this case; is that correct?

24 A. I had no direct involvement with ibrutinib. I -- I
25 don't know that I didn't see the paper from Sonic. I

Swift - cross

1 usually read drug and design. I'm sure that I saw that
2 title at least in the table of contents.

3 Q. You had no specific knowledge of ibrutinib prior to
4 June 4, 2012; correct?

5 A. That's -- I had no specific knowledge. I think that's
6 probably fair to say.

7 Q. And you never made any form of ibrutinib?

8 A. No.

9 Q. You've never performed any analytical tests on any
10 form of ibrutinib?

11 A. No.

12 Q. And you have never tested ibrutinib capsules or
13 tablets; is that correct?

14 A. That's correct.

15 Q. Now, you have never performed any polymorph screening
16 or crystallization experiments on ibrutinib?

17 A. I performed plenty of polymorph screenings on other
18 compounds but I never performed them on ibrutinib.

19 Q. You've never actually ever seen a sample of ibrutinib;
20 is that right?

21 A. That's correct.

22 Q. Now, Dr. Swift, ibrutinib capsules and tablets are a
23 commercial embodiment of claim 5 of the '455 patent; is that
24 correct?

25 A. My understanding is that that drug product is used in

Swift - cross

1 those commercial products, yes.

2 Q. Now, none of the anticipation theories that you have
3 testified about are express anticipation theories; is that
4 correct?

5 A. They're -- now you are talking legal terms. I'm a
6 scientist, so when you talk, when you use the word express,
7 my understanding is there is express and inherent. It may
8 not be on the, in the four corners of the documents Pollyea
9 and Fowler, but I do think common sense dictates that if you
10 are using a, if you are delivering a drug to patients in a
11 clinical study, you must have gone through the exercise of
12 identifying a stable form.

13 If you don't have it in a stable form, you might
14 as well throw out all of your data from a clinical study
15 because it's not going to be worth very much.

16 So knowing that you disclosed a Phase 1 study
17 helping somebody to put in that work, there's no possible
18 way in which that work wasn't done. So it may not be
19 explicitly in the documents, but there's no scenario that I
20 can perceive of where it is not inherently in those
21 documents.

22 Q. So let's take a step back for a moment because in
23 order for something to be anticipated, each and every
24 limitation of the claims of the '455 patent have to be
25 either disclosed expressly or inherently in the reference

Swift - cross

1 that you are pointing to.

2 Do you understand that?

3 MR. GUTMAN: Objection, Your Honor. It calls
4 for a legal conclusion.

5 THE COURT: Overruled.

6 BY MS. BHARKHDA:

7 Q. Dr. Swift, do you understand that?

8 A. I understand that is what you just told me, yes.

9 Q. Is that the analysis you applied when you performed
10 your validity analysis in the case?

11 A. That it needs to be expressly or inherently
12 anticipated, yes, that's the analysis that I used in this
13 case.

14 Q. And you are not claiming that each and every
15 limitation of claim 5 of the '455 patent is expressly
16 disclosed in either Fowler or Pollyea; is that correct?

17 A. I'm not saying that it's expressly disclosed, but I do
18 believe that it is inherently disclosed just based on common
19 sense.

20 Q. And the only two references that you are relying on as
21 anticipatory references for claim 5 of the '455 patent are
22 Pollyea and Fowler; is that right?

23 A. When I did my literature search, I found multiple
24 references. I could probably have cited other, other
25 references, but I thought that Pollyea and Fowler were

Swift - cross

1 sufficient to demonstrate prior disclosure of form A.

2 Q. So the opinions that you have actually offered in this
3 case regarding anticipation are limited to anticipation
4 based on Pollyea and anticipation based on Fowler; is that
5 correct?

6 A. Yes, I think that's in the report.

7 Q. And you understand that in order for there to be
8 inherent anticipation, each and every limitation of claim 5
9 of the '455 patent must necessarily be present in Pollyea
10 and Fowler; is that right?

11 A. Yes.

12 Q. So it can't be probably or possibly or likely present.
13 It has to be necessarily present; is that right?

14 A. Yes.

15 Q. Now, let's discuss the Pollyea reference first.

16 Now, Dr. Swift, in rendering your opinion, you
17 reviewed the '455 patent, JTX-9; is that correct?

18 A. Yes.

19 Q. And you understand that the face of the '455 patent
20 contains a references cited section that begins on the first
21 page? And if we could have JTX-9, that might help.

22 A. Yes. There's a very long list of references cited.

23 MS. BHARKHDA: And, Mr. Brooks, can you please
24 go to JTX-9-10. I'm omitting the leading zeros to reduce
25 the wordage. Okay. And can you please highlight the

Swift - cross

1 reference to Pollyea.

2 BY MS. BHARKHDA:

3 Q. Dr. Swift, Pollyea is listed in a references cited
4 section on the face of the '455 patent, JTX-9; correct?

5 A. Yes, I believe that's the same reference, although
6 it's not a complete reference. It's not published in -- if
7 you have the Pollyea reference, can you remind me which?

8 Q. The Pollyea reference in DTX-467.

9 A. So that is not exactly the same reference as DTX-467,
10 and I doesn't contain all of the information.

11 Q. Dr. Swift, I'm not sure I understand. Actually, can
12 you explain that to me?

13 A. My Pollyea reference is a publication in Blood from
14 2009 and the reference that you have highlighted on that
15 slide, there's no indication that that corresponds to the
16 reference from Blood.

17 Q. It has the same title.

18 A. It has the same title.

19 Q. And it has the same year.

20 A. Title and year are not necessarily indicative that
21 they are the same document.

22 Q. I understand. Did you actually pull the poster
23 abstract from the 51st annual meeting and exhibition that's
24 referred to on the face of the '455 patent?

25 A. If all I have is that snippet from the '455 patent, I

Swift - cross

1 don't know how to get that. Where am I supposed to find
2 that?

3 Q. My question was: Did you look for it? Did you, for
4 example, ask counsel to find it for you?

5 A. I did not ask counsel to find that reference for me,
6 no.

7 Q. And did you look for it yourself?

8 A. Again, I just said I don't know how to find an
9 incomplete reference.

10 Q. You consider a poster abstract to be an incomplete
11 reference?

12 A. The way that's written there, that's an incomplete
13 reference. I don't even know what journal. Not all poster
14 abstracts are reproduced in journals, so I would not have
15 any knowledge that this is published somewhere. Just
16 referring to a poster abstract doesn't help me with that.

17 Q. So you would not be able to -- so you can't tell from
18 this whether or not the Pollyea referred to on the '455
19 patent is the same poster abstract that is published in the
20 Blood journal 2009 that you are looking at?

21 A. Based on the similarity of the title, I would not
22 think that they are -- that it is impossible that they refer
23 to the same thing, but that's different than what you asked
24 me. You asked me if this is the same thing and I told you
25 that based on what's written in the '455 patent, that I

Swift - cross

1 don't know where to find that reference because it's an
2 incomplete reference.

3 Q. But the Patent Office considered a Pollyea reference
4 with the identical title to the one that you relied on from
5 the identical year with the identical abstract number; is
6 that correct?

7 A. Apparently, yes.

8 Q. And the title specifically mentions PCI 367 -- 32765;
9 is that correct?

10 A. It does.

11 Q. And so the fact that a reference is listed on the
12 front of the patent means that the Patent Office considered
13 it during prosecution of the patent; is that right? Excuse
14 me. A reference is listed on the front of the patent means
15 that the Patent Office considered it during prosecution of
16 the patent.

17 MR. GUTMAN: Okay, Your Honor. It calls for a
18 legal conclusion. Lacks foundation.

19 THE COURT: I'm going to sustain the objection.

20 BY MS. BHARKHDA:

21 Q. Now, Dr. Swift, there are numerous references listed
22 in the publications section of the references cited of the
23 '455 patent that use the code PCI-32765. Correct?

24 A. You know, nobody wants to spend their time reading
25 them all, but I can see just below that, there's another one

Swift - cross

1 that says PCI-32765, so I assume there are multiple
2 references that refer to PCI-32765.

3 Q. And, in fact, if you look in the publication section,
4 there are over 40 publications listed there that contain the
5 phrase PCI-32765 in their title; isn't that right?

6 A. Yes.

7 Q. So the references cited section of the '455 patent,
8 let's say the references that were provided to the examiner
9 during prosecution contain dozens of references to
10 PCI-32765; is that correct?

11 A. Well, again, I have not counted them, so I'm going to
12 take your characterization of this as being dozens as true
13 and I do this and I assume that you are telling me the truth
14 here. Nobody wants me to sit here and count, but I will
15 assume that what you are telling me is factually correct,
16 and so then I have to agree with your statement.

17 Q. And the Patent Office granted the patent application
18 any way?

19 A. Yes, the patent was granted.

20 Q. So the Patent Office did not conclude that mere
21 disclosures of the phrase PCI-32765 disclosed form A and
22 all of the 2-Theta limitations in claim 5 of the '455
23 patent?

24 MR. GUTMAN: Objection, Your Honor. Lacks
25 foundation.

Swift - cross

1 THE COURT: Well, I mean -- actually, what was
2 the question? Hold on. Sustained.

3 BY MS. BHARKHDA:

4 Q. So, Dr. Swift, let's talk about the version of Pollyea
5 that you walked through during your testimony.

6 MS. BHARKHDA: Mr. Brooks, can we have DTX-467,
7 please.

8 BY MS. BHARKHDA:

9 Q. So DTX-467 is not a version of Pollyea that would have
10 been available to a person of ordinary skill in the art at
11 the time of the June 4, 2012, priority date for the '455
12 patent; is that correct?

13 A. No, it was available in May of 2010. Why would it not
14 be available in 2012?

15 Q. DTX-467 was actually generated in 2020; is that
16 correct? It's a printout from the Internet from 2020?

17 A. It may have been printed out in 2019, but if you ask
18 was I -- in 2012? No, I would have no reason to print this
19 out in 2012.

20 Q. So it was printed out in 2019 or 2020 to the best of
21 your knowledge?

22 A. To the best of my knowledge, yes.

23 Q. And, in fact, if you look, there is a list of articles
24 at the end of the second page and there's a reference there
25 to an article dating from 2020.

Swift - cross

1 Do you see that?

2 A. Yes, I see that.

3 Q. So DTX-in order for an article from 2020 to be, from
4 2020 to be included in DTX-467, the document could not have
5 been printed before 2020; is that correct?

6 A. I understand the reason, yes.

7 Q. And you don't know whether DTX-467 represents the
8 version of Pollyea that would have been available to a POSA
9 as of June 4th, 2020 -- 2012?

10 A. I -- I remember you asking me questions about this in
11 the deposition and I cannot tell you what a journal does on
12 their on line platform. I assume that it's reasonable that
13 they would update relevant articles at the end, but the
14 actual article itself ends where the copyright 2009 by the
15 American Society of Hematology is listed. Whatever updates
16 get done to that article to draw attention to more recent
17 literature is what I would expect to be the only part of
18 this that changes with time.

19 Q. But you didn't actually go and attempt to get the
20 version of Pollyea that would have been in the literature
21 publicly available to a person of ordinary skill in the art
22 prior to June 4, 2012; is that correct?

23 A. You're asking an impossible task. You cannot do that.
24 I should say I know of no way to do what you are asking.

25 Q. Did you make any requests to any library for the

Swift - cross

1 actual version of Blood from the relevant month in 2009 in
2 order to obtain the version of the article that would have
3 been provided, that would have been available to a POSA in
4 2012?

5 A. No, I didn't, but if this is going to be an issue,
6 then it's going to be a big problem going forward because
7 there are many journals that are only published on line, not
8 in print edition.

9 Q. But you didn't make an attempt to actually get the
10 hard copy version of the article that would have been
11 available to a POSA in 2012?

12 A. No. It didn't occur to me to do that because I don't
13 see how that is relevant.

14 Q. Okay. And so you relied on this 2020 Internet
15 printout of the article to render your opinion about what a
16 POSA would have known from that article as of June 4th,
17 2012?

18 A. Yes.

19 Q. And your opinion is the mere mention of the code name
20 PCI-32765 would have inherently disclosed to a person of
21 ordinary skill in the art prior to June 4th, 2012, that each
22 and every one of the elements of claim 5 of the '455 patent
23 was present; is that right?

24 A. Yes, that's true, because the PCI-32765 is being used
25 in this reference as part of a Phase 1 dose escalation

Swift - cross

1 study, and if you are doing a clinical trial, you have put
2 that drug into a stable form, and when you go through the
3 documents that must be behind this Phase 1 study, the
4 clinical study report, the IND documents, it must correspond
5 to form A. The fact that claim 5 cites six powder X-ray
6 diffraction lines, you don't have just six -- six X-ray
7 diffraction lines on their own don't publication. The fact
8 that six refraction lines reflect an inherent property of
9 form A is what's important. So, yes, this reference
10 discloses, the PCI-32765 is used in a Phase 1 dose
11 escalation study and that that is a form A which has, which
12 necessarily has all of the claims that are being asserted.

13 Q. So I just want to make sure I understand. Are you
14 saying that PCI-32765 as you reviewed in that particular
15 study is form A or that PCI-32765 in all circumstances
16 always and necessarily is form A of ibrutinib?

17 A. In every Phase 1 study that I am aware of, it is
18 necessarily form A.

19 Q. Okay. But only in the context of Phase 1 study?

20 A. That's -- this reference only discloses a Phase 1
21 study, so I'm limiting my opinions to what existed in this
22 Phase 1 study.

23 Q. So your opinions are limited to the dosage forms used
24 in the Phase 1 study of Pollyea?

25 MR. GUTMAN: Objection, Your Honor.

Swift - cross

1 THE COURT: Overruled.

2 THE WITNESS: Are people waiting for me?

3 THE COURT: Doctor, so the question pending to
4 you is, so your opinions are limited to the dosage form used
5 in the Phase 1 study of Pollyea.

6 THE WITNESS: I don't think it's limited to
7 Pollyea. We have other references as well that report on
8 this Phase 1 dose escalation study. I'm simply saying that
9 what is disclosed in these studies indicates form A and all
10 the properties of form A, which include the fact that it is
11 the most stable form, that it has those powder diffraction
12 lines.

13 I don't know how it -- I'm probably not
14 answering your question, but I don't know how to answer your
15 question.

16 BY MS. BHARKHDA:

17 Q. You are not offering the opinion that the code name
18 PCI-32765 in and of itself inherently and necessarily and
19 always discloses to a POSA that you are talking about
20 crystalline form A ibrutinib; is that right?

21 A. I think a POSA in 2012, all of the available
22 information that I could get that talks about how PCI-32765
23 is used in clinical studies responds, corresponds to form A.

24 Q. So, Dr. Swift, I understand that you keep repeating a
25 limitation to clinical studies, but that is not my question.

Swift - cross

1 What I'm asking about is: Does the code name PCI -- would
2 the code name PCI-32765 prior to June 4th of 2012 have
3 necessarily and always meant crystalline form A of ibrutinib
4 with the six claimed peak of the '455 patent?

5 A. I am aware that ibrutinib can exist in multiple
6 polymorphic forms. My understanding is that in clinical
7 studies, it has always benefited from (inaudible).

8 Q. But ibrutinib exists in other crystalline forms; is
9 that correct?

10 A. It existed in other less stable forms which convert to
11 form A.

12 Q. Now --

13 A. The other forms cited in the, in other crystal form
14 patents in the family, but those require more specialized
15 conditions to obtain them and they readily convert. That
16 was part of some of the other documents that have been, part
17 of the other studies that have been done. That's what he
18 said, he tested form B and C and they both converted to A.

19 Q. But not in all instances?

20 A. No. He identified some very specialized conditions
21 which would not allow it, which would -- where it would
22 not convert quickly, but in the vast majority of conditions,
23 he said that it was easy to obtain and other forms converted
24 to it.

25 Q. Now, prior to June 2012, amorphous ibrutinib also

Swift - cross

1 existed; is that correct?

2 A. Yes, I believe it did. But amorphous forms are less
3 stable than crystalline form. When you know there's a
4 stable crystalline form available, amorphous ibrutinib
5 converts to crystalline form A.

6 Q. Now, is it your opinion and testimony that amorphous
7 ibrutinib converts to crystalline form A in all
8 circumstances?

9 A. It may not convert in all circumstances. If you take
10 it down to 0 Kelvin, my guess is that nothing 0 Kelvin
11 converts. I would not say all conditions convert, but I
12 would say the vast majority of conditions that people would
13 be working on, amorphous form ibrutinib would readily
14 convert to form A, particularly, put one tiny little seed
15 crystal into that mixture. I would expect that would
16 catalyze the transformation to form A.

17 Q. So prior to June 4, 2012, there were six forms, six
18 crystalline forms of ibrutinib and an amorphous form of
19 ibrutinib available to the inventor; correct?

20 MR. GUTMAN: Objection. Lacks foundation.

21 THE COURT: Overruled.

22 THE WITNESS: I -- again, I don't know if it was
23 exactly six and an amorphous form. I will take that on face
24 that that is accurate.

25 BY MS. BHARKHDA:

Swift - cross

1 Q. Well, there are six forms that were disclosed in the
2 patent, the filing date for which is June 4, 2012; is that
3 correct?

4 A. Yes. I just won't be an expert on other patents that
5 might exist should there be anything else.

6 Q. So there -- it would be accurate to say there are at
7 least six, there were at least six crystalline forms and one
8 amorphous form available to the inventor prior to June 2012;
9 is that right?

10 A. Yes, but, again, as I said yesterday, only one form
11 can be the most stable form.

12 Q. Right. Claim 5 of the '455 patent doesn't contain any
13 limitation to a thermodynamically stable form; is that
14 correct?

15 A. No. It just happens that the powder X-ray diffraction
16 pattern line corresponds.

17 Q. We know that because the inventor made form A. Is
18 that correct?

19 THE COURT: So, Dr. Swift, we lost your voice.
20 Sorry. All right. You said, no. It just happens that the
21 powder X-ray diffraction pattern line corresponds, and then
22 we lost everything you said, so do you remember what you
23 were saying?

24 All right. So the question -- let me do this.
25 There was a question put to you: Claim 5 of the '455 patent

Swift - cross

1 doesn't contain any limitation to the thermodynamic stable
2 form; is that correct?

3 And you said, no. It just happens that the
4 powder X-ray diffraction pattern line corresponds.

5 THE WITNESS: To the thermodynamically stable
6 form.

7 THE COURT: Okay. Thank you very much.

8 THE WITNESS: Sorry. I don't know what
9 happened.

10 THE COURT: That's okay. That's the limitation
11 of technology.

12 Go ahead. Ms. Bharkhda, I guess you want to
13 pick up.

14 MS. BHARKHDA: Sure.

15 THE COURT: Then you said we know that because
16 the inventor made form A; is that correct?

17 MS. BHARKHDA: Thank you, Your Honor.

18 BY MS. BHARKHDA:

19 Q. Dr. Swift, we know that form A is the most, is
20 currently the most thermodynamically known form of ibrutinib
21 because the inventors made the form and then tested it
22 relative to the other form, forms and determined which one
23 was the most thermodynamically stable known se forms; is
24 that right?

25 A. The inventors did characterize all of the forms and

Swift - cross

1 based on what they found, they concluded that form A was the
2 thermodynamically stable form.

3 Q. But before form A was made, when, for example, only
4 form B existed, form B was the most thermodynamically stable
5 form of the known forms of ibrutinib or the existing forms
6 of ibrutinib; is that correct?

7 A. I'm not sure that that is true. I -- I introduced the
8 '444 patent previously. That patent disclosed how to
9 synthesize ibrutinib. It disclosed that you could use
10 conventional methods to crystallize it and re-crystallize
11 it. I think it's very likely given the relative stability
12 of form A and amorphous form that you are referring to, that
13 there's amorphous -- that there's form A in the product.

14 Q. But you are not making any of your inherent
15 anticipation arguments on the '444 patent; is that correct?

16 A. I did not talk about that patent in the context of
17 that -- for the testimony for the Court. That's correct.

18 Q. Okay. So, but the fact that we now know today that
19 form A is the most thermodynamically stable form of
20 ibrutinib that we know, it's based on the work of the
21 inventor; is that correct?

22 A. It's based on the inventors, but it's also based on
23 the outside analysis that was performed to do the polymorph
24 screen. Some of those people who did the screen weren't
25 listed as inventors, as I recall.

Swift - cross

1 Q. So it's all based on Pharmacyclics' work to make the
2 form, characterize them and figure out which one is the most
3 thermodynamically stable?

4 A. They are the ones that are developing the drug, so,
5 yes.

6 Q. And before the crystalline forms of ibrutinib were
7 made, a person of ordinary skill in the art could not have
8 known which ones would be the most thermodynamically stable;
9 correct?

10 A. I think a POSA would look at the molecule and readily
11 assume that it's crystallizable based on its chemical
12 structure; they would be motivated to do a screen and based
13 on that screen, they would also inevitably create form A,
14 and if they create other forms and do a comparison of their
15 relative stability, they would deduce that form A is a
16 thermodynamically stable form.

17 Q. My question was different. My question was: Before
18 crystalline forms of ibrutinib had been made, a POSA could
19 not have predicted which one would be the most
20 thermodynamically stable.

21 A. No. You have to do the -- that's correct. You have
22 to do the experiment to figure out which one is the
23 thermodynamically stable form.

24 Q. And a POSA, there is no disclosure in the art prior to
25 June 2012 that form A of ibrutinib is the most

Swift - cross

1 thermodynamically stable known form of ibrutinib; correct?

2 A. It's not form A until somebody decides to call it form

3 A. A thermodynamically stable form by any other name would
4 still be a thermodynamically stable form.

5 Q. There's no disclosure that a crystalline form with the
6 properties of crystalline form A was the most

7 thermodynamically known form prior to June 2012. There's no
8 disclosure about which -- whether you call it form A or form

9 X or form Y, there is no discussion in the art of what was
10 the most thermodynamically stable form of ibrutinib; is that
11 correct?

12 A. That's correct, but I think you're misconstruing this,
13 because I don't think that citing six powder X-ray
14 diffraction lines necessarily talk about some property.

15 It's not talking about its melting points. It's not talking
16 about -- it's simply telling you what the structure is, so
17 it's not measurable from the --

18 Q. Those six lines, those six X-ray powder diffraction
19 lines were disclosed in the art the first time in the
20 application that led to the '455 patent; correct?

21 A. That's -- it is the case, I think, that that was the
22 first time that those powder diffraction lines were cited.

23 Q. Now, let's talk about Pollyea for a second. Pollyea
24 doesn't identify what chemical compound PCI-32765 is; is
25 that correct?

Swift - cross

1 A. When I found this, I will say that when I did my
2 literature search and I found this article among many
3 others, many others included PCI-32765 in the title. Many
4 of those other articles gave you a molecule that identified
5 PCI 33765 like the Honigberg 2010 maybe that I just showed a
6 little bit ago.

7 Q. Dr. --

8 A. I don't know the order, whether I looked at Pollyea
9 before I looked at Honigberg before I looked at any other
10 reference.

11 Q. Well, that was not my question. I just want to know
12 what is in Pollyea? Pollyea does not identify what chemical
13 compound PCI-32765 is.

14 A. I think it does.

15 Q. Point me to where in Pollyea, in the actual document,
16 DTX-467, the article identified what chemical compound
17 PCI-32765 is.

18 A. The way it's used in every sentence indicates that it
19 is the drug substance. Right? If I'm giving somebody a
20 drug, I know that's a molecule, and so even if I -- I will
21 grant you that it does not say, it does not give you the
22 long IEPAC chemical name of the compound and it does not
23 draw the structure out for you, and the fact that it doesn't
24 draw it out could be because this is a limited size. It
25 doesn't give that.

Swift - cross

1 Q. But when you read, when a POSA reads PCI-32765,
2 they're going to understand that it's a molecule and that
3 molecule will be given structure, but they won't know what
4 the molecule in a given structure is from reading the words
5 PCI or the phrase PCI-32765?

6 A. No, but I assume a POSA is sufficiently intelligent to
7 be able to figure out what that refers to.

8 Q. Now, Pollyea doesn't contain the chemical name for
9 PCI-32765?

10 A. Right, but, again, for all the same reasons that I
11 just said, a POSA would be able to figure it out without --
12 with very little effort.

13 Q. Now, Pollyea doesn't mention crystalline form A of
14 ibrutinib in any way, does it?

15 A. Not expressly, no, but inherently, it does.

16 Q. Pollyea doesn't even mention crystalline form of
17 ibrutinib; is that correct?

18 A. Not explicitly, though when you say it's being
19 delivered as an oral drug, I believe it does disclose that
20 crystalline forms are present.

21 Q. But an oral dosage form could be amorphous; is that
22 correct?

23 A. It could be, but my experience with oral drugs are
24 delivered as crystalline forms and not method forms.

25 Q. Most, but not all; is that right?

Swift - cross

1 A. Most, but not all.

2 Q. And there would not have been any sort of regulatory
3 or legal prohibition on using an amorphous form in a Phase 1
4 trial for a drug substance; correct?

5 MR. GUTMAN: Objection. Lacks foundation.

6 THE COURT: Overruled.

7 THE WITNESS: I don't know that -- I don't know
8 of any specific requirement that it must be a crystalline
9 form, but, again, when I look at the chemical structures of
10 the molecule, my intuition based on years of experience and
11 based on what I think a POSA would know is that they would
12 have every confidence that that molecule was crystallize
13 able and given that crystalline forms are more stable than
14 amorphous forms, they would be motivated to put it in a
15 crystalline form.

16 So, yes, if I make an assumption in this Phase 1
17 study it is being delivered in crystalline form, that
18 reflects my own personal experience based on lots of other
19 compounds.

20 BY MS. BHARKHDA:

21 Q. You said, and part of that is based on you looking at
22 the chemical structure for ibrutinib; is that right?

23 A. Yes.

24 Q. And that's not disclosed in Pollyea; is that correct?

25 A. No, but, again, like I said, it wouldn't take much

Swift - cross

1 work to figure out what the chemical structure is. It
2 certainly didn't take me much work to figure out what the
3 structure is.

4 Q. Now, and one wouldn't be able to tell simply from the
5 mention of a solid oral form whether or not the actual
6 dosage being used was amorphous or crystalline; is that
7 correct?

8 A. That is technically correct, although, like I said,
9 given that most drugs are delivered in crystalline form, a
10 POSA would likely assume that it's being delivered in
11 crystalline form.

12 Q. Pollyea does not teach a POSA how to make crystalline
13 form A of PCI-32765 of ibrutinib; is that correct?

14 A. That's correct. It's simply using it. It's not
15 teaching you how to make it.

16 Q. And it doesn't teach you how to make crystalline, any
17 crystalline forms of PCI-32765?

18 A. That's correct. It's just using something that has
19 already been made.

20 Q. And Pollyea contains no XRPD data; is that correct?

21 A. That's also correct, but the XRPD data is just an
22 inherent property of the material they are using.

23 Q. Now, Pollyea doesn't identify the protocol number for
24 the Phase 1 dose escalation study that it's talking about;
25 is that correct?

Swift - cross

1 A. I believe that's true, but I also know that any Phase
2 1 steady must have a clinical study behind it, a clinical
3 study protocol behind it.

4 Q. Now, just to confirm, a POSA reading Pollyea wouldn't
5 have a firm position that, or, excuse me, a firm opinion
6 that PCI-32765 was crystalline form A of ibrutinib; is that
7 correct?

8 A. I think it depends on what you mean by firm. I said
9 that my assumption would be that a POSA would assume that
10 you could make this into a crystalline form, so my
11 assumption is that if I'm a POSA in 2012, my assumption is
12 this is a different form.

13 If you want me to assume that it's an amorphous
14 form, I probably need additional information that would make
15 me think that it's amorphous. Otherwise, my default
16 position is going to be I'm going to assume that it's
17 crystalline.

18 Q. Do you recall giving deposition testimony in this
19 case?

20 A. Oh, yes.

21 Q. And I took your deposition in August; is that correct?

22 A. Yes, for many, many, many hours.

23 Q. And that was just about two months ago?

24 A. Yes.

25 Q. Okay. And do you recall testifying then that you

Swift - cross

1 didn't know whether a POSA would have a firm opinion on
2 whether or not PCI-32765 was crystalline form A of
3 ibrutinib?

4 A. Vaguely.

5 Q. So during your deposition, you testified that a POSA
6 would not have a firm opinion regarding whether PCI-32765 is
7 a crystalline form of ibrutinib; is that correct?

8 A. I think at the deposition, I didn't challenge your
9 definition of what firm means, and I've been very careful
10 just now to say that my assumption is that it would be
11 crystalline.

12 So I think it comes down to what you want to
13 call it as firm, you know. Do we want to talk about this in
14 terms of probability. Right? You've got a one in a million
15 chance, is that firm, is that not firm? You've got a one in
16 ten chance, is that firm or is that not firm. So I think my
17 testimony in deposition is not -- is exactly what I'm saying
18 here. We're just maybe parsing the boundaries of what firm
19 means.

20 MS. BHARKHDA: Now, Mr. Brooks, can we please
21 play Dr. Swift's deposition testimony starting from lines,
22 from line, 222:14 to 223:11.

23 (The videotape deposition clip was played as
24 follows.)

25 Question. Now, Dr. Swift, looking only at the

Swift - cross

1 disclosure of Pollyea 2009, not considering any other
2 outside documents, does Pollyea 2009 disclose whether
3 PCI-32765 is amorphous or crystalline?

4 "Answer: If I read the introduction, it says
5 PCI-32765 is an oral, potent selective covalent inhibitor.
6 And since it's an oral, oral to me suggests that it's a
7 solid. The fact that it's in a Phase 1 dose escalation
8 study suggests that it's stable.

9 "And I think I would need to know something
10 about the -- if I'm a POSA, I'm going to assume that the
11 oral form is a stable form; otherwise it wouldn't be in a
12 Phase 1 study. Beyond that, I don't know that a POSA would
13 have a firm ibrutinib on whether it is crystalline form A,
14 for example.

15 "But I think actually it would be fairly
16 reasonable to assume that if it's a stable form, it's more
17 likely than not to be a crystalline form because crystalline
18 forms are known to be more stable than amorphous forms."

19 (End of video clip.)

20 MR. GUTMAN: Your Honor, objection as improper
21 impeachment.

22 THE COURT: Well, I mean, I thought it was a
23 little odd at the time we were just playing a deposition,
24 but you didn't object at the time, so it's kind of like a
25 late objection. You know, I mean, kind of the cat is out of

Swift - cross

1 the bag.

2 MR. GUTMAN: Your Honor, to the extent they want
3 to move that testimony into evidence, it's not a prior
4 inconsistent statement because it's improper impeachment.

5 THE COURT: Well, wait a second. What do you
6 mean it's not a prior inconsistent statement?

7 MR. GUTMAN: It's not, it's not proper
8 impeachment, so --

9 THE COURT: Well --

10 MR. GUTMAN: Ms. Bharkhda hasn't shown that Dr.
11 Swift's testimony that she just played is inconsistent with
12 what she testified here.

13 THE COURT: I don't know. I mean, I can go back
14 and look at the transcript, I guess. I mean, this is not
15 the norm that I see a deposition played. Normally, the
16 witness is confronted with, didn't you say and then the
17 witness denies she says it. It's played. I mean, this is
18 made even more difficult because we're remote.

19 I don't know that there's even a move --

20 THE WITNESS: Am I allowed to make any comments?

21 THE COURT: No, no. Just hold up, Doctor. This
22 is lawyers stuff. In fact, Sanji, you should have this as a
23 sidebar, so let's move Dr. Swift to a waiting room so the
24 lawyers can talk with me privately. Thank you.

25 All right. Give me a second. Let me go back

Swift - cross

1 and look.

2 So, you know, Ms. Bharkhda, we can't just play a
3 deposition. You've got to lay the foundation. You've got
4 to --

5 MS. BHARKHDA: Your Honor, I apologize if you
6 didn't think I did that. I did that by asking Dr. Swift if
7 she thought a POSA would have a firm opinion about whether
8 PCI-32765 is crystalline form A.

9 THE COURT: Right. But I mean what happened
10 was, she said we're kind of parsing what firm is. You guys
11 had a discussion back and forth reminiscing about your
12 lengthy deposition in August, and then -- hold on. Let me
13 just find the transcript.

14 MS. BHARKHDA: Your Honor, I believe actually
15 the testimony she provided is clearly inconsistent. The
16 testimony she provided at her deposition was clearly
17 inconsistent with the testimony she just gave regarding that
18 opinion.

19 THE COURT: All right. Just give me a second
20 here. I'm putting you all on mute for a second so I can ask
21 the court reporter something.

22 Okay. Having reread the transcript, I think
23 this was appropriately played as an inconsistent statement
24 given the answer that Dr. Swift had. So the prior
25 inconsistent statement made under oath, the objection is

Swift - cross

1 overruled. Let's bring Dr. Swift back.

2 All right. You can bring Dr. Swift back in.

3 You can resume questioning.

4 BY MS. BHARKHDA:

5 Q. Now, Dr. Swift, a person of ordinary skill in the art
6 would have understood prior to June 4, 2012, that a drug
7 product could use a metastable crystalline form of a drug
8 substance; is that correct?

9 A. Yes.

10 Q. And here, for example, crystalline form B of ibrutinib
11 would be considered a metastable form of ibrutinib?

12 MR. GUTMAN: Objection, Your Honor. Outside the
13 scope.

14 THE COURT: All right. Hold on.

15 THE WITNESS: Yes. Form B --

16 THE COURT: Any way, it's overruled. Go ahead.

17 THE WITNESS: I'm sorry. I thought you --

18 THE COURT: No, no. You're right. Well, we're
19 all talking over each other because of the remoteness. The
20 objection is overruled, so, Dr. Swift, you should go ahead
21 and answer the question.

22 THE WITNESS: So that's what I thought I was
23 answering, that you, you asked me if B was metastable and,
24 yes, I agree that B is metastable.

25 BY MS. BHARKHDA:

Swift - cross

1 Q. And crystalline form B of ibrutinib would be
2 considered a metastable form of ibrutinib; is that correct?

3 A. That's correct.

4 Q. Now, Dr. Swift, your opinions relating to the Fowler
5 reference, DTX-148, they are essentially the same as your
6 opinion for the Pollyea reference; is that correct?

7 A. That's correct.

8 Q. So there's nothing unique to Fowler that is not
9 contained in Pollyea that you believe would inherently
10 anticipate claim 5 of the '455 patent?

11 A. Yes, that's correct. Fowler, an update to the ongoing
12 study.

13 Q. Now, can we look at DTX-148 itself, the version of
14 Fowler that Dr. Swift used on her direct examination?

15 DTX-418, Dr. Swift, that's also the version that
16 you used when you were doing your anticipation analysis in
17 forming your opinions in this case; is that right?

18 A. I believe so.

19 Q. But DTX-148 is an Internet printout from 2019;
20 correct?

21 A. Again, I don't know if it's 2019 or 2020, but it would
22 have been one of those two years.

23 Q. So DTX-148 itself is not the of Fowler that would have
24 been available to a person of ordinary skill in the art
25 prior to June 12, 2012; is that correct?

Swift - cross

1 A. I don't know exactly what would have been available in
2 2012 because I did not look at this document printed in
3 2012, but there's nothing in this abstract or in the two
4 pages here that is, that relates to any new content since
5 2012, so I have no reason to believe this wouldn't be what
6 somebody in 2012 would be looking at.

7 Q. You didn't make any attempt to actually obtain the
8 version of Fowler that was published in the literature prior
9 to 2012; is that correct?

10 A. I did not, but I was also not aware that that would be
11 a thing, that anybody would not -- that anybody would
12 question the validity of an oral that I'm able to pull in
13 real time now being something that was the same or different
14 from ten years ago.

15 Q. But you understood you were supposed to put yourself
16 in the shoes of a person of ordinary skill in the art as of
17 2012 and accept the information that would have been
18 available to them; is that right?

19 A. I do understand that.

20 Q. To confirm, Dr. Swift, Fowler does not identify a
21 protocol number for the Phase 1 dose escalation study that
22 it discusses. Is that correct?

23 A. I think that's correct.

24 Q. And not --

25 A. Not explicitly.

Swift - cross

1 Q. And it doesn't disclose a chemical name for PCI-32765?

2 A. Not explicitly, no.

3 Q. And it doesn't identify the chemical compounds that,
4 for PCI-32765?

5 A. No, but as I said, with Pollyea, if you know
6 PCI-32765, it does not take very much work to figure out
7 what the chemical structure is contained in the four corners
8 of this document.

9 Q. And Fowler doesn't mention crystalline form A of
10 ibrutinib; is that correct?

11 A. No, it does not mention it explicitly.

12 Q. And it doesn't say anything about the physical form of
13 PCI-32765 that was used in the Phase 1 study; is that
14 correct?

15 A. Well, it makes reference to the fact that it's orally
16 bioavailable, so beyond the fact that it's being delivered
17 orally, it does not specify which form had been explicitly.

18 Q. And Fowler contains no XRPD data; is that correct?

19 A. That's correct. In the study, they are just receiving
20 the samples and using them to deliver them to patients.
21 They would have no reason to do XRPD on the sample.

22 Q. Now, none of the references that you discussed in your
23 direct examination that were publicly available prior to
24 June 4, 2012 contain the phrase crystalline form A of
25 ibrutinib; is that correct?

Swift - cross

1 A. I think that's correct.

2 Q. None of the references that you discussed in your
3 direct examination that were publicly available prior to
4 June 4th, 2012 contained any X-ray powder diffraction data
5 for any form of ibrutinib; is that correct?

6 A. That is correct if you are limiting it to explicitly
7 identifying, yes.

8 Q. And none of the references you discussed in your
9 direct examination that were publicly available prior to
10 June 4, 2012, contain mention of ibrutinib with XRPD peaks
11 at 5.7, 13.6, 16.1, 18.9, 21.3 and 21.6 degrees 2-Theta plus
12 or minus 0.1; is that correct?

13 A. I believe the references inherently disclose it but
14 they don't explicitly disclose it.

15 Q. Now, one of the documents that you talked about, one
16 of the references that you talked about on direct was
17 JTX-77.

18 MS. BHARKHDA: Mr. Brooks, can we put up JTX-77.
19 Actually, if you can pull up Dr. Swift's slides, Alv J S 17.
20 Okay.

21 BY MS. BHARKHDA:

22 Q. So you have on your slide 3 two pages of the document.
23 Right? We have one document displayed over the cover page
24 of JTX-77?

25 A. Yes.

Swift - cross

1 Q. Okay.

2 MS. BHARKHDA: Mr. Brooks, can we please bring
3 up JTX-77 itself. In the portion of the cover on the slide
4 we have a confidentiality statement saying that the
5 information in JTX-77 is confidential and proprietary to
6 Pharmacyclics; is that right?

7 A. Yes, but I've never shared this information with
8 anybody outside this case.

9 Q. Now, JTX-77 is an internal confidential Pharmacyclics
10 document; is that right?

11 A. I actually don't, I don't know whether that's right or
12 wrong. But based on the confidentiality statement and the
13 fact that it's a Pharmacyclics document, I actually -- I
14 don't know.

15 Q. You mentioned, I think, in your testimony on direct
16 examination that you performed literature searches as part
17 of your analysis in the case; is that correct?

18 A. That's correct.

19 Q. You did not obtain JTX-77 through one of those
20 literature searches; is that correct?

21 A. No, I could not have obtained that on my own, but when
22 I found based on the literature that I did find, I asked
23 counsel if there were underlying documents and if I had the
24 ability to get those documents.

25 Q. And then they provided the Pharmacyclics documents

Swift - cross

1 that were produced by plaintiffs in this case to you to
2 answer that question; is that right?

3 A. Yes.

4 Q. Now, and to confirm, you have no basis to believe that
5 JTX-77 would have been publicly available to a person of
6 ordinary skill in the art prior to June 4th, 2012; is that
7 correct?

8 A. You know, I don't know how Pharmacyclics treats their
9 confidential documents. If somebody was interested in this,
10 would they decide to share it? Would the coordinating
11 investigator decide to share it? I don't know. I don't
12 know those people. I don't know what their policy is. I
13 expect that they would say, no, it's confidential, we're not
14 going to share it, but if somebody decides to share it for
15 some other reason, I don't know.

16 Q. You have not seen anything that JTX-77 was, in fact,
17 shared by Pharmacyclics on a nonconfidential basis prior to
18 June 4, 2012; is that correct?

19 A. That's correct.

20 Q. And you don't know when JTX-77 was created; is that
21 correct?

22 A. Well, at the bottom of the page it says it was
23 approved in February 2017, so I assume I'm afraid it's
24 before that date. I assume a document of this length is not
25 created in a day and that there were several drafts

Swift - cross

1 available of this prior to that date. But it covers the
2 study that went from 2009 to 2012.

3 Q. And according to JTX-77, the study was completed after
4 June 4, 2012; is that correct?

5 A. Yes.

6 Q. And the document date of February 27, 2013, is after
7 June 4, 2012; is that correct?

8 A. That's correct.

9 MS. BHARKHDA: Now, can we please have DTX-1514,
10 please, Mr. Brooks.

11 BY MS. BHARKHDA:

12 Q. So this is the other document that you relied on to
13 indicate that PCI-32765 would have been understood to
14 necessarily disclose form A of ibrutinib; is that correct?

15 A. Yes.

16 Q. Now, the cover page of DTX-1514 similarly has a
17 confidentiality statement like JTX-77; is that right?

18 A. That's correct.

19 Q. And as far as you know, JTX-1514 is a confidential
20 internal Pharmacyclics document?

21 A. That's what I assumed it means when it has the
22 confidentiality statement on the front cover.

23 Q. And you did not find DTX-1514 in any of your
24 literature; is that correct?

25 A. Correct. This is not publicly available.

Swift - cross

1 Q. And it would not have been publicly available to a
2 person of ordinary skill in the art prior to June 4, 2012;
3 is that correct?

4 A. That's true.

5 Q. And can we have Dr. Swift's slide 19.

6 So, Dr. Swift, you took us to slide 19 during
7 your direct testimony and indicated that the page that was
8 the chart, table 21 that we're showing from DTX-1514,
9 indicates to you that PCI-32765 is always associated with
10 crystalline form A of ibrutinib; is that correct?

11 A. It is always associated with crystalline form A and in
12 every clinical study that's done.

13 Q. But in table 21 on DTX-1514, we can see that you have
14 one batch in the top of Table 1 that is not highlighted.

15 Do you see that?

16 MS. BHARKHDA: Mr. Brooks, can we put a box
17 around that box, which is in the exactly upper -- yes.
18 There we go.

19 BY MS. BHARKHDA:

20 Q. So this is the box that describes batch 072097.

21 Do you see that?

22 A. I see that.

23 Q. And that's actually form B of ibrutinib; is that
24 correct?

25 A. That non-clinical batch is form B and it's a lot

Swift - cross

1 number that was not used in the clinical study.

2 Q. But here, Table 1, table 21 is using the code
3 PCI-32765 to refer to form B of ibrutinib; is that correct?

4 A. The content in the blue box there corresponds to form
5 B.

6 Q. And that is listed under the heading PCI-32765?

7 A. That's how they chose to put it in the table.
8 Probably easier to put it in the table that way than it is
9 to have a separate table for 1, 1 lot number.

10 Q. So even within Pharmacyclics, PCI-32765 was used to
11 refer to both form B and form A of ibrutinib; is that
12 correct?

13 A. You know, I don't know. Does this lot number
14 corresponding to form B? I don't know how Pharmacyclics
15 talked about it, but they are making the distinction in this
16 table that there is form A and form B of this compound.

17 Q. So there's form A of PCI-32765 and form B of
18 PCI-32765?

19 A. Form B, it's my understanding it's not even a single
20 form. It's a mixture, or at least it's referred to as being
21 a mixture. The content that refers to it as form B or
22 polymorph B, I don't remember the exact terms. I don't want
23 to be on the record. I shouldn't talk about this. There's
24 form A and form B in this table, but every clinical batch
25 and every batch that was used in that dose escalation study

Swift - cross

1 is identified as form A.

2 Q. And all of that is referred to as PCI-32765?

3 A. Again, if that's how you want to interpret the
4 table, that's fine. Like I said, they could have just put
5 that in there to avoid making a whole other table for one,
6 one batch.

7 Q. And documents from Pharmacyclics from the relevant
8 time period also use the code PCI-32765 when they are just
9 talking amorphous ibrutinib; is that correct?

10 A. I don't -- I can't speak confidently about in which
11 every way they refer to amorphous form because I was focused
12 on form A.

13 Q. So you didn't look into the question of how the term,
14 of whether or not the term PCI-32765 was used within
15 Pharmacyclics to amorphous ibrutinib?

16 A. I'm sure I looked at it, but I didn't really think
17 about it deeply.

18 Q. Because you were focused on form A?

19 A. Yes.

20 Q. All right. DTX-1514, if we can go back to the cover
21 page, Mr. Brooks, that has a date of August 27, 2012? Do
22 you see that?

23 A. August 17th.

24 Q. Thank you for the correct. August 17th, 2012.

25 Do you see that?

Swift - cross

1 A. Yes.

2 Q. So that document also dates after the June 4th, 2012,
3 date of the patent application?

4 A. Yes.

5 Q. Now, we also talked about, I think you referred to the
6 Zvonicek article, DTX-1700. DTX-1700 was not available to a
7 POSA prior to June 4th of 2012; is that correct?

8 A. That's correct.

9 Q. And if we can look at the experimental section of
10 DTX-1700. Okay. So the authors of DTX-1700 made forms A, B
11 and C in 2018 by following the procedures described in the
12 '455 patent; is that correct?

13 A. That's correct.

14 Q. And then they used forms A and B to conduct further
15 polymorph screening; is that right?

16 A. Yes, that's correct.

17 MS. BHARKHDA: Now, can we go to the section
18 3.1.3, evaluation of the methods, Mr. Brooks.

19 THE COURT: Can we take a break? Let's just
20 hold for one second, would you, please? Hold on just one
21 second.

22 So I've also got a technical issue. That's what
23 I was trying to deal with. I just lost something on my
24 computer screen.

25 I will tell you what. Let's take -- I mean, is

Swift - cross

1 this a good time or do you want a couple minutes and then
2 we'll break in terms of the flow of examination? Where are
3 we?

4 MS. BHARKHDA: Your Honor, we can take a break
5 now if you would like. Then, hopefully, actually, I can,
6 you know, streamline some things and we'll keep it as
7 efficient as we can when we come back.

8 THE COURT: Why don't we do that. Why don't we
9 break then until 10:45. All right? All right. Thank you.

10 (Short recess taken.)

11 - - -

12 (Proceedings resumed after the short recess.)

13 THE COURT: Okay. I'm here. Is everybody else
14 here? It looks like it. Okay. All right, counsel.

15 BY MS. BHARKHDA:

16 Q. Dr. Swift, were you present for opening statements on
17 Tuesday?

18 A. No, I wasn't.

19 Q. You didn't attend. You talked a bit about X-ray
20 powder diffraction and X-ray powder diffraction 2-Theta
21 peaks.

22 Do you agree that 2-Theta peaks in an X-ray
23 powder diffraction provides structural information about the
24 crystalline form of the polymorph at issue?

25 A. Yes.

Swift - cross

1 Q. I want to talk about some of the references that you
2 discussed during your opening, excuse me, during your direct
3 examination.

4 So I believe that you, you referred to Bauer
5 2008; is that correct?

6 A. Yes.

7 Q. And that was DTX-1008; is that right?

8 A. I don't know. I have to find it.

9 MS. BHARKHDA: Mr. Brooks, can we pull up
10 DTX-1008 to make it easier.

11 THE WITNESS: Yes, it is 1008.

12 BY MS. BHARKHDA:

13 Q. Okay. Now, I believe you described Bauer as a general
14 reference that would provide guidance that would lead one to
15 perform a polymorph screen or polymorph search I believe as
16 you said yesterday; is that right?

17 A. Yes. This is a pretty general article.

18 Q. It does not mention ibrutinib or PCI-32765; is that
19 correct?

20 A. That's correct.

21 Q. And it provides no specific guidance on how to make
22 crystalline forms of ibrutinib; is that correct?

23 A. That's correct. There's no mention of ibrutinib in
24 this, in this report, in this document.

25 Q. And Fowler, in essence, says that one should use their

Swift - cross

1 technical know-how and their individual know-how about the
2 compound they are working with to design a set of
3 experiments, execute those experiments and then test the
4 result of those experiments; is that right?

5 A. That's right, later he offers this advice for every
6 pharmaceutical that would be in development.

7 Q. And let's look at Miller 2007. We'll just find the
8 right number for that one.

9 I believe it's DTX-1657. Can we have that one,
10 Mr. Brooks?

11 And Miller is also a general reference that
12 is not in any way specific to ibrutinib or PCI-237651;
13 correct?

14 A. It's the general reference that should apply to --
15 most pharmaceuticals are all homocyclic.

16 Q. It provides no specific teaching about crystallization
17 experiments or conditions for ibrutinib or PCI-32765?

18 A. The word ibrutinib does not appear in that document,
19 no.

20 Q. And I believe you pointed us to the solvent table in
21 Miller?

22 A. Yes.

23 Q. Let me just find the right table number. I apologize.
24 Table 3.

25 MS. BHARKHDA: Mr. Brooks, can we go to Table 3?

Swift - cross

1 I believe it begins on the base number beginning 761. There
2 we go. Table 3 of Miller spans numerous pages of the
3 reference; correct?

4 A. That's right.

5 Q. It contains over 120 solvents; is that right?

6 A. I didn't count them, but that's probably right.

7 Q. And I think you indicated that a POSA might choose to
8 use all of these solvents when conducting crystallization
9 experiments relating to a particular compound; is that
10 right?

11 A. They might, but, again, it depends on how much time
12 and money and interest you have. If you have unlimited
13 time, interest and money, why not use all solvents. Most of
14 us don't work in that environment, so you would be judicious
15 and use a smaller subset of the entries in this table, the
16 screen.

17 Q. And so if you don't have unlimited time, money and
18 resources, a person of ordinary skill in the art who was
19 attempting to perform crystallization experiments on a new
20 drug compound would have to make a decision about which
21 solvent to use and whether to potentially combine some of
22 the solvents on this table?

23 A. They would, but, you know, right below the Table 3
24 heading, it offers up that the bold solvents would be a
25 smaller subset of one set a POSA wouldn't want to focus on.

Swift - cross

1 Q. So a POSA could potentially stick to just stick to
2 testing the bolded solvent here in a crystallization
3 experiment; is that right?

4 A. They could.

5 Q. Or they could use the bolded solvents and some other
6 solvents that they use from the list; is that correct?

7 A. Correct, but I think the way that you embark on a
8 polymorph screening experiment is not that you start from
9 the infinite number of solvents and you whittle your way
10 down. You start with a small number of solvents and you
11 throw it out.

12 Q. And there are a number of factors that affect the, or
13 that one could use when conducting a polymorph screen or a
14 polymorph search; is that correct?

15 A. There are a number of variables one could probe. I
16 think solvents and temperature are the two easiest ones to
17 look at and those would be the first two that a POSA would
18 reasonably assess.

19 Q. And there was no teaching or, no teaching in the art
20 prior to June 4th, 2012, about how any of those particular
21 variables would apply to or should be used with ibrutinib;
22 is that correct?

23 A. The general information available that a POSA would
24 know on how to approach the problem, but, no, you're not
25 going to find a document that tells you exactly which

Swift - cross

1 solvents to try because that's the purpose of doing
2 experiments. Why would you do an experiment if it's already
3 done?

4 Q. Now, Dr. Swift, one of the other references that you
5 talked about during your direct examination is the '444
6 patent.

7 Do you recall that?

8 A. Yes.

9 Q. Okay.

10 MS. BHARKHDA: And, Mr. Brooks, can we have the
11 '444 patent? I believe it's DTX-1. And if you could go to
12 the second page DTX-one.

13 BY MS. BHARKHDA:

14 Q. And the references cited on the face of the '444
15 patent, the '444 patent appears. You can see it there in
16 the upper right corner of the first page of content of the
17 patent.

18 MS. BHARKHDA: Mr. Brooks, can we hone in on it
19 up in the right-hand corner underneath the patent number?
20 I actually meant to go to JTX-9. Thank you for correcting
21 me.

22 BY MS. BHARKHDA:

23 Q. So this is the '455 patent, and on the face of it,
24 have listed the '444 patent that you discussed in your
25 testimony; is that correct?

Swift - cross

1 A. Yes.

2 Q. And so the '444 patent was submitted to the Patent
3 Office during prosecution of the '455 patent?

4 A. Yes.

5 Q. Now, the '444 patent does not mention crystalline form
6 A of ibrutinib; is that correct?

7 A. The '444 patent offers crystallization and
8 recrystallization as common methods to purify any of the
9 compounds that were listed in that compound patent. Among
10 them was ibrutinib, but it does not specifically call out
11 form A.

12 Q. And the '444 patent contains no X-ray diffraction
13 data; is that correct?

14 A. It doesn't contain X-ray diffraction data, but it
15 references standard characterization methods, which would
16 include X-ray powder diffraction.

17 Q. Now, a POSA would understand that the specification of
18 the '444 patent only generally discusses different
19 crystalline forms without disclosing how to make any
20 specific crystalline form; is that correct?

21 A. In general, that's correct, but I will say that the
22 word crystal, crystallization and recrystallization appear
23 in the text of this document a remarkable number of times.

24 Q. I understand. I want you to -- I would like you to
25 answer the question that I asked though. A POSA would

Swift - cross

1 understand that the specification of the '444 patent only
2 generally discusses different crystalline forms without
3 disclosing how to make any specific crystalline form?

4 A. Yes, it generally discusses how to make crystalline
5 forms.

6 Q. Without disclosing how to make any specific
7 crystalline form; is that correct?

8 A. I don't know. If it offers you a recipe, if you
9 decide to call it a recipe, the fact that you have crystal
10 form or doesn't it?

11 Q. So is it your testimony that the '444 patent discloses
12 how to make a specific crystalline form?

13 A. It's not telling me how to make a specific crystal
14 form, but it's telling me how to do it.

15 Q. Okay. So --

16 A. That doesn't make any sense. I'm sorry. It's giving
17 me general information on how to purify my compounds, which
18 are solids, crystalline, but it's not giving you a specific
19 route to obtain form A, B, C or any, any other form of any
20 of the drugs in the, in the, that the patent covers.

21 Q. And, finally, I think you talked in your direct
22 examination about Honigberg 2010. Can we have Honigberg
23 2010. I believe it's DTX-28. And DTX-278 does not contain
24 any specific teaching about how to make any crystalline form
25 of ibrutinib; is that correct?

Swift - redirect

1 A. It does not explicitly tell you how to make any forms
2 of ibrutinib, that's correct.

3 Q. And it doesn't specifically reference crystalline
4 forms of ibrutinib?

5 A. I would need to read it. I believe that's true.

6 MS. BHARKHDA: Thank you, Your Honor. I have no
7 further questions for Dr. Swift.

8 THE COURT: All right. Redirect.

9 REDIRECT EXAMINATION

10 BY MR. GUTMAN:

11 Q. Dr. Swift, how many Phase 1 dose escalation studies
12 for ibrutinib were undertaken?

13 A. There's only one as far as I know.

14 Q. Is your opinion that Pollyea and Fowler anticipate
15 claim 5 of the '455 patent based on the disclosure of
16 PCI-32765 in the context of that Phase 1 dose escalation
17 study of ibrutinib?

18 A. Yes.

19 Q. Is that different from answering the question of what
20 is PCI-32765 in any and all contexts?

21 A. I think that's a different question.

22 Q. Are you -- as part of your anticipation argument for
23 Pollyea and Fowler, is it your argument that for -- excuse
24 me. Is it your opinion that PCI-32765 is form A in any and
25 all contexts?

Swift - redirect

1 A. Depending on how somebody is using PCI, using the
2 term, I wouldn't say that it is form A in every context, but
3 it is certainly form A in the context of the Phase 1 dose
4 escalation study.

5 Q. And how do you know that?

6 A. Because behind any Phase 1 study there must be study
7 protocol, and the study protocols identify specific lot
8 numbers which can be traced back to specific batches, which
9 can be traced back to specific characterization data, and
10 when I looked at that that characterization data, it was
11 with every single batch that was used in that those, in dose
12 escalation studies corresponding to form A, and form A
13 necessarily, inherently has the six powder diffraction lines
14 that are cited in claim 5 that has been asserted.

15 Q. Now, Ms. Bharkhda asked you some questions about a
16 citation to an abstract in the '455 patent that she
17 suggested is Pollyea.

18 Do you recall that?

19 A. I do recall that.

20 Q. Are you aware of any information that was available to
21 the Patent Office in considering whether to issue into the
22 '455 patent that was identical to the information that you
23 analyzed in forming your opinion that Pollyea and Fowler
24 anticipate claim 5 of the '455 patent?

25 A. I wasn't in the Patent Office, so I don't know

Swift - redirect

1 the total of the documents that they saw or didn't see. I
2 have no knowledge to what they, what they had at their
3 disposal.

4 Q. The clinical trial report and the IND documents that
5 you analyzed to correlate the batch numbers with what
6 crystalline form PCI-32765 was in the Phase 1 dose
7 escalation studies, are you aware of whether those documents
8 were considered by the Patent Office in addressing the
9 Pollyea reference that Ms. Bharkhda pointed to?

10 A. I have no knowledge of that, but I imagine if they
11 were considered, they would be in the materials that were
12 considered.

13 MR. GUTMAN: Can we go to DTX-467, please.

14 BY MR. GUTMAN:

15 Q. Now, Dr. Swift, is there any doubt in your mind about
16 whether the information pertaining to the abstract in
17 DTX-467 was published in November of 2009?

18 A. I have no reason to doubt that.

19 Q. And when a POSA would want to obtain an abstract or a
20 scientific article given the existence of computers and
21 technology, would a POSA typically obtain such a publication
22 from a database or would they go physically to a library to
23 obtain the article?

24 A. In this day and age, people don't use the library very
25 much.

Swift - redirect

1 MS. BHARKHDA: Your Honor, okay. I was on mute.
2 I'm sorry. I'm late. The question is leading, it lacks
3 foundation and is outside the scope of the opinion that Dr.
4 Swift offered in the case.

5 THE COURT: I think you opened the door.
6 Overruled.

7 BY MR. GUTMAN:

8 Q. Now, I want to take this Pollyea reference section by
9 section. The title through the introduction of the
10 reference, is there any doubt in your mind that that was
11 published by November 20th, 2009?

12 A. No.

13 Q. Now, can we go to patients and methods through result,
14 if you can make it there. Okay?

15 Is there any doubt in your mind that the
16 patients and methods and results sections were published as
17 of November 20th, 2009?

18 A. No.

19 Q. Can we continue, please. Now, is there any doubt in
20 your mind that the conclusion through the disclosure section
21 was published as of 2009?

22 A. No.

23 Q. And what does that copyright scan at the bottom tell
24 you?

25 A. The copyright tells me that that is the publication

Swift - redirect

1 date.

2 Q. Now, are the -- see the topics section there?

3 A. Yes.

4 Q. And if you can scroll up, please, or, I'm sorry,
5 scroll down. I apologize. Okay.

6 And in including these citations that Ms.
7 Bharkhda pointed to, some of which are after 2009, do you
8 see that?

9 A. I do.

10 Q. Are those simply the results of the obtaining this
11 article online as opposed to obtaining the abstract from a
12 printed copy in the library?

13 A. That's my assumption. If you had a printed copy in a
14 library, it would not contain those potential articles of
15 interest.

16 Q. Did you rely on any of those articles of interest or
17 any other part of Pollyea 2009 that was not part of Pollyea
18 2009 that was published in November of 2009 in forming your
19 opinions that Pollyea 2009 anticipates claim 5 of the '455
20 patent?

21 MS. BHARKHDA: Objection Your Honor.

22 THE COURT: Hold up. The question is did you
23 rely on any of those articles of interest or any other part
24 of Pollyea 2009 that was not part of Pollyea 2009 that was
25 published in November of 2009 in forming your opinions that

Swift - redirect

1 Pollyea 2009 -- and you have an objection for what? Based
2 on what?

3 MS. BHARKHDA: Lack of foundation and
4 speculation at least. Dr. Swift said she had no idea of
5 what the actual version of Pollyea 2009 looked like, so how
6 could she make a comparison about that with what she
7 actually looked at?

8 Mr. Gutman is asking me to compare a document we
9 have with a document that she says she has never seen.

10 THE COURT: Okay.

11 MS. BHARKHDA: Your Honor, I will point out,
12 Mr. Gutman said that the topics section of the article would
13 have been part of the 2009 article and we don't think that's
14 true.

15 MR. GUTMAN: I --

16 THE COURT: Hold up. Actually, I will tell you
17 what we'll do. Let's put Dr. Swift in the waiting room,
18 please. And tell me when that's done.

19 So let's just talk about this generally, because
20 I've got the funny feeling this may come up again.

21 Let's figure out just generally, I think, you
22 who we're going to deal with this situation, which is a
23 product of living in the Internet world, potentially, maybe
24 not.

25 So, look, if there's going to be extrinsic

Swift - redirect

1 evidence that is going to call into question the
2 authenticity of the documents, and by authenticity, I mean
3 whether or not the documents printed out from the Internet
4 in 2020 is actually the abstract or the poster, and I'm kind
5 of curious what those two things mean because I'm actually,
6 you know, not exactly sure. I was going to ask the witness
7 myself.

8 But if there is something like that, then that
9 is going to be very probative and I'm going to admit it.
10 For instance, one of the articles was, one of the two
11 exhibits were where these types of issued had been raised
12 was authored at least in part by Honigberg.

13 Now, I assume, Ms. Bharkhda, you've got access
14 to Honigberg; correct?

15 MS. BHARKHDA: Your Honor, I believe the two
16 references for this, in fact, were Fowler and Pollyea.

17 THE COURT: Hold on, please. I'm not so sure
18 about that. Hold on.

19 So you think the two articles are -- yes, so
20 Pollyea. What is the exhibit number?

21 MS. BHARKHDA: The exhibit number for Pollyea is
22 467.

23 THE COURT: All right. So hold on. Let me just
24 look at it.

25 MS. BHARKHDA: DTX.

Swift - redirect

1 THE COURT: Okay. So my reading of it is
2 Honigberg is listed as one of the authors of this.

3 MS. BHARKHDA: Yes, Your Honor.

4 THE COURT: So my question is: You have access
5 to Honigberg; right? You do. He's the inventor. You have
6 access.

7 MS. BHARKHDA: He's no longer, he's no longer an
8 employee of the company or anything like that.

9 THE COURT: That's not really my question.
10 Look, do you have access? Did you guys represent him during
11 his deposition?

12 MS. BHARKHDA: Yes.

13 THE COURT: You have access to him.

14 MS. BHARKHDA: We have access to Dr. Honigberg.

15 THE COURT: All right. Let's always try to cut
16 to the chase so I don't have to probe on things like that.
17 You've got access to him.

18 My point would be, it would be probative, in
19 fact, it would be killer, killer testimony if Dr. Honigberg
20 came in and said, you know what? Dr. Swift has the wrong
21 article, DTX-0467 didn't exist in this form back in 2009
22 and, you know, that would be killer. Otherwise, it's just
23 just cute cross-examination in my book.

24 Unless you want to tell me differently, maybe
25 you're going to bring in another document that shows, this

Swift - redirect

1 iteration of the document, and I'm not counting the, you
2 know, the print line that says it was whether it was
3 printed. I'm not counting the fact that there are potential
4 articles of interest that postdate 2009. That was clearly
5 out. I'm talking about the substance of the article. That
6 would be damning evidence, potentially. Right?

7 Do you have something like that?

8 MS. BHARKHDA: So, Your Honor, so if I could
9 take a step back, I think our main concern about what is in
10 this printout, what is in DTX-467 that we do not believe was
11 in the original article is the topic section that links to
12 other key words.

13 THE COURT: All right. Hold up. So where is
14 the topic section?

15 MS. BHARKHDA: On the second page.

16 THE COURT: I just found topic.

17 MS. BHARKHDA: That section was not in the
18 article.

19 THE COURT: What's the evidence of that? What
20 is the evidence of that?

21 MS. BHARKHDA: We ordered the original copy --

22 THE COURT: My point is, that's going to be
23 killer evidence. I get that. That's really good evidence.
24 That's what I meant by -- I only gave Honigberg as an
25 example because I see his name on top and I'm thinking, oh,

Swift - redirect

1 maybe you're going to walk in with Honigberg.

2 So that is helpful to me to understand this.

3 Okay.

4 MS. BHARKHDA: But, Your Honor --

5 THE COURT: Then I'm kind of at a loss with why
6 you want to preclude her testimony on this, because you're
7 going to come in and contradict it.

8 MS. BHARKHDA: I -- I don't think we're actually
9 asking to preclude her testimony on it. I think the issue
10 is, as the defendants presenting evidence on invalidity in
11 this case, Alvogen has the burden to produce the relevant
12 prior art and establish that what they are showing in the
13 report is prior art and they have not done that and also in
14 our, in the deposition, we pointed this out to her two
15 months ago in front of Alvogen's counsel. We pointed out
16 the fact that this is not the right, this is not the version
17 of the article that a POSA would have had.

18 THE COURT: Right.

19 MS. BHARKHDA: And they have done nothing do
20 correct it.

21 THE COURT: Here's the thing.

22 MS. BHARKHDA: We don't think they can meet
23 their burden.

24 THE COURT: You are objecting to questions, I
25 think, by Mr. Gutman. Basically, he's asking Dr. Swift, do

Swift - redirect

1 you have any doubt, and I think it's kind of peculiar how
2 she could have no doubt whatsoever, frankly. I question
3 that. Right? She pulled it off the Internet.

4 But putting that aside, he's asking her this
5 series of questions. Do you have any doubt what? That the
6 introduction section was part of it. You're going to bring
7 in a witness that shows that part of these articles were not
8 there. I'm just wondering why I'm, like, trying to figure
9 out whether there's a foundation for this question, and I
10 wanted to take a sidebar because I'm going to guess, like, I
11 didn't see anything on the face of the other document, like
12 Honigberg's name that might suggest, oh, my gosh, we really
13 have the wrong article here.

14 Okay. So hold on. So now with all of that
15 background and now having a better sense of why you are
16 calling into question the authenticity of this document,
17 which I get now, let me think.

18 So the question here, though, is: Did Dr. Swift
19 rely on any of the articles of interest. Right? And you've
20 established and the document itself establishes that at
21 least some of those documents postdate the June 2012 date.

22 So did you rely on any of those articles or any
23 part of Pollyea that was not part of Pollyea in November of
24 2009 that was published in 2009?

25 Right. There is no foundation. I see your

Swift - redirect

1 point now. It's that we don't know if she ever looked at
2 the original article. Right. Okay.

3 I'm going to sustain the objection then and you
4 can't ask that question. There has been no foundation that
5 she established -- I mean, Mr. Gutman, can you point me to
6 anywhere in the record where it was established that she saw
7 the original Pollyea 2009?

8 MR. GUTMAN: Your Honor, I think the foundation
9 that I would lay with her is that a scientist, a POSA who
10 prints out an article from the Internet knows what part of
11 the article was in the original, you know, print version
12 versus what part of the article is the product of just
13 merely printing it out on the Internet.

14 THE COURT: Okay. You know what I'm going to
15 do? I'm going to let you ask that question. I will tell
16 you why. Because I think you are doing what I think you
17 hurt yourself with your prior expert witness when you gave
18 that witness, and I don't know whether you personally,
19 instructions about the PTO regs, and then the witness ends
20 up opining based on an incomplete understanding of PTE regs,
21 because, you know, at the end of the day, it's a trial, and
22 at the end of the day when I have in front of me competing
23 expert evidence, I have to make a credibility determination
24 based on what is in front of me, and I'm going to tell you.
25 Whoever it was that educated Dr. Lepore about the patent

Swift - redirect

1 examination and had him put in his slide deck, that very
2 much negatively affected his credibility.

3 If you want to ask this witness whether she's
4 able to look at the Internet and figure out based on that
5 whether information was in or not in the original published
6 document, go for it, because I think you are -- you know,
7 I've already said.

8 So actually, Ms. Bharkhda, I hear your point, I
9 take it, but I actually am not even sure it's in your
10 interests to grant the objection. I am overruling the
11 objection.

12 Mr. Gutman, you can proceed at your peril.

13 MR. GUTMAN: Your Honor, may I explain?

14 THE COURT: No, you may not. Let's move on and
15 you can address it at the next break. Let's just move on
16 because of the witness. You can object and say whatever you
17 want. All right?

18 BY MR. GUTMAN:

19 Q. Dr. Swift, I want to go back to DTX-467, which is
20 Pollyea 2009. Can you please describe for me what portions
21 in this actual document you believe were published in
22 November 2009 and provide the basis for that conclusion?

23 A. So my opinion is that I would expect in 2009 the
24 publication would include the title, the author's name, the
25 abstract, the introduction, patients and methods, the

Swift - redirect

1 results, the conclusion, the disclosure, and most likely,
2 the author notes with the asterisk indicating the names of
3 the deciding member and a copyright symbol with 2009 by the
4 American Society of Hematology. That's what I would be
5 confident in as being available, in 2009.

6 Q. And what's your basis for that understanding, Dr.
7 Swift?

8 A. Because all of those components would be part of the
9 original abstract, and that is what would be in published
10 form.

11 The topics section that appears above the author
12 notes may or may not have been in that original publication
13 in 2009. It's above other notes, which I could, I would
14 guess, and it would be a total guess, means that it was
15 available in 2009, but the fact that the font is in a
16 different color makes me uncertain, so I don't want to claim
17 to have firm knowledge of whether the topic is available or
18 isn't available.

19 Anything that comes after author notes is
20 unavailable, which is kind of obvious since all of that
21 material postdates 2009.

22 MR. GUTMAN: Your Honor, I want to address
23 something, but I want to make sure that I can do so given
24 the circumstances that we're doing this remotely, so I would
25 like to have the witnessing into a different room to be able

Swift - redirect

1 to address a particular issue with you.

2 THE COURT: All right. That's a good idea.

3 All right, Dr. Swift, we're going to excuse you
4 again.

5 THE WITNESS: Okay.

6 THE COURT: All right. Go ahead, Mr. Gutman.

7 MR. GUTMAN: Thank you, Your Honor.

8 So I'm just going to hold this up. This is a
9 print copy of Pollyea 2009.

10 THE COURT: Okay.

11 MR. GUTMAN: And we repeatedly asked plaintiffs,
12 because we thought it was silly, their objection, quite
13 honestly, because substantively, it's exactly the same, it's
14 exactly the same as the printed version substantively.

15 And they never called into question the
16 substance of any of it, and so we told them that if they had
17 a problem, we'll just replace out the copies, because
18 substantively, it's exactly the same. And when we were
19 putting together our exhibit list, they refused to allow us
20 to do that.

21 And so that's why we're left in this situation
22 and we're spending just an inordinate amount of time
23 addressing something that is undisputed. It is undisputed
24 that the substance is exactly the same.

25 So I have this Pollyea article. I can give it

Swift - redirect

1 to the witness. I can bring up a comparison between this
2 and the, you know, the version that we're looking at that is
3 an exhibit, and we can go through and show that
4 substantively, it's exactly the same.

5 THE COURT: Okay. But the only thing is -- I
6 mean, that can be done at this point, but why keep this
7 witness when she said she has never laid a foundation that
8 she has seen this original article?

9 MR. GUTMAN: She can say that substantively.

10 THE COURT: I can do that myself, or, counsel,
11 you guys can close that out in your closing documents if
12 they're the same or they're different.

13 MR. GUTMAN: Well, there are indicia that this
14 was pulled from the published journal article.

15 THE COURT: But it sounds like the other side is
16 going to introduce the original article any way.

17 Ms. Bharkhda, what's your position on this?

18 MS. BHARKHDA: I mean, Your Honor, we have no
19 problem with the actual version of Pollyea coming in,
20 particularly because it shows the topics that were included
21 in the version that Dr. Swift used and relied on were not
22 part of the original article. There was no reference to
23 ibrutinib or NHL or any of the answers listed in the topic
24 section.

25 It's not the article that the witness was using

Swift - redirect

1 and relied on in forming her opinions, but we don't have any
2 objection to it coming in as an exhibit, but I don't think
3 it's relevant for Mr. Gutman to show it to the witness
4 because she has never seen it before and has no foundation
5 for it.

6 THE COURT: It sounds like you both will agree
7 to stipulate to the admissibility of the article and then we
8 can have the attorneys argue whether or not they're the same
9 or different in that regard, and I don't need to do this
10 through this witness.

11 It doesn't sound like she has any knowledge of
12 the original article in any event. Right?

13 MS. BHARKHDA: Correct.

14 THE COURT: Mr. Gutman, why don't you just save
15 it and you can stipulate to the admission of the article and
16 then you guys are free to argue if it's significant.

17 MR. GUTMAN: Thank you, Your Honor.

18 THE COURT: Thank you. That was smart to do
19 that outside the presence of the witness. Thank you.

20 You can bring the witness back in, please.

21 MR. GUTMAN: Can we bring up DTX-148.

22 BY MR. GUTMAN:

23 Q. Dr. Swift, I would like to go through the same
24 exercise as we did with Pollyea and to have you identify
25 what on this document you believed was published by November

Swift - redirect

1 of 2010.

2 Can we start at the top?

3 A. I think you would see the title, the author's name,
4 the abstract. She would state an introduction. The pts and
5 methods, the results. Table 1 would be included. The
6 conclusions would be included. The disclosures would be
7 included.

8 And, again, I don't know what to make of the
9 topics because it's in a different color, but I assume that
10 the copyright 2010 by the American Society of Hematology
11 would be included.

12 It's only the font that's in red there that I'm
13 not certain about.

14 Q. And you didn't rely on the information in the topics
15 section as part of your opinion that Fowler anticipates
16 claim 5 of the '455 patent?

17 A. No, I did not.

18 Q. Is stability of form A an inherent property of form A,
19 whether that's disclosed in the prior art or not?

20 A. Yes, it is.

21 Q. Why is that?

22 A. Because the stability is a function of the crystal
23 form. It's inherent. It's not separable from that firm.

24 Q. Can we bring up JTX-0001.

25 When did the '444 patent issue, Dr. Swift?

Swift - redirect

1 A. April 7th, 2009.

2 Q. And you pointed to some discussion in the '444 patent
3 that crystallization and characterization and purification
4 were described as conventional; is that correct?

5 A. Described as conventional several times in this
6 document.

7 Q. Now, can we bring up Pollyea again, DTX-467.

8 Now, DTX-467, which is Pollyea, when did Pollyea
9 2009 publish?

10 A. 2009.

11 Q. What month?

12 A. November.

13 Q. Okay. Is that after when the '444 patent issued?

14 A. It is after when the '444 patent issued.

15 Q. So would a POSA prior to April, or, sorry, prior to
16 2012 have had available both the '444 patent as well as
17 Pollyea?

18 A. Yes.

19 Q. In your opinion, would a POSA reading Pollyea,
20 especially in light of the '444 patent, be able to make
21 crystallized and characterized ibrutinib?

22 MS. BHARKHDA: Objection, Your Honor. I believe
23 either outside the scope of any of Dr. Swift's reports. She
24 never indicated that a POSA would combine or look to the
25 '444 patent in order to understand Pollyea.

Swift - redirect

1 MR. GUTMAN: Your Honor --

2 THE COURT: Let's excuse Dr. Swift. Sorry about
3 this, Doctor. The joys of litigation.

4 If we could excuse Dr. Swift. Thank you.

5 All right. Mr. Gutman, where is it in the
6 report?

7 MR. GUTMAN: No, Your Honor. I don't, I don't
8 know that it's in the report, but Ms. Bharkhda opened a door
9 because what she was questioning Dr. Swift on was whether a
10 POSA -- what she was really getting at is whether Pollyea is
11 enabled for ibrutinib, and she asked questions of Dr. Swift
12 about whether Pollyea teaches someone how to make ibrutinib,
13 and what she is really getting at is that Pollyea is not
14 enabling for ibrutinib.

15 And so this is this is in response to that line
16 of questions from Ms. Bharkhda. And I will also not that --

17 THE COURT: Hold on. I'm sorry. I'm sorry I'm
18 slow on some of these things. It's just a lot to digest.

19 Did Dr. Swift testify that the patent is invalid
20 for lack of enablement?

21 MR. GUTMAN: No, Your Honor.

22 THE COURT: Let's just assume for argument's
23 sake during the cross-examination, the witness was asked
24 questions about implicitly at least whether Pollyea enabled
25 the invention. Why does it matter?

Swift - redirect

1 MR. GUTMAN: Well, what plaintiffs will probably
2 argue in their post-trial briefing, you, is Pollyea is not
3 enabled for making ibrutinib.

4 THE COURT: Wait.

5 MR. GUTMAN: If they --

6 THE COURT: Hold on. Stop, stop, stop. I have
7 to digest what you just said. Okay. They are going to say
8 it's not enabled or they are just going to say it doesn't
9 disclose the subject matter because, among other things, it
10 doesn't teach how to make ibrutinib. Isn't that a different
11 question?

12 MR. GUTMAN: Well, I think what plaintiffs are
13 getting at and Ms. Bharkhda can tell us whether this is not
14 plaintiffs' position, but in order for an anticipatory
15 reference to anticipate, it has to be enabling for what it
16 teaches.

17 THE COURT: Okay.

18 MR. GUTMAN: And so I believe that plaintiffs
19 will argue in their post-trial briefing that Pollyea is not
20 enabling for ibrutinib and as an attempt to try to remove it
21 as an anticipatory reference.

22 THE COURT: Okay.

23 MR. GUTMAN: And so Ms. Bharkhda was asking Dr.
24 Swift questions about whether in the context of Pollyea,
25 whether Pollyea taught how to make ibrutinib, which is going

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1 to the enablement question.

2 And so the questions that I was asking Dr. Swift
3 was in response to that line.

4 THE COURT: Okay. Before we hear from Ms.
5 Bharkhda, let me ask you both something. I actually, I've
6 never had to deal with anticipation as a judge, so one thing
7 I'm just confused about, frankly, is, to read something into
8 Pollyea 2009, you have to incorporate something twice in the
9 '444 patent. Why aren't we in obviousness as opposed to
10 anticipation?

11 MR. GUTMAN: Well, Your Honor, I think Dr. Swift
12 testified that Pollyea anticipates because by referring to
13 PCI-32765 in the context of the Phase 1 dose escalation
14 study, that inherently discloses within the four corners
15 that PCI-32765 is crystalline form A ibrutinib that will
16 have inherently the peaks that form A has.

17 THE COURT: But I mean, so, and I caught,
18 there's obviously -- even the plaintiffs had questions. I
19 will learn about that. But it seems to me if you're -- if
20 by inherent, the theory is you bootstrap other prior art,
21 why don't you move into obviousness at that point? What am
22 I missing?

23 MR. GUTMAN: Because under the theory of
24 inherency, Your Honor, inherent anticipation, the literature
25 references that you rely on to demonstrate what is inherent

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1 need not be prior art, and, in fact, there's no requirement
2 that the inherency within the anticipatory reference needed
3 to have even been recognized by a POSA as of the priority
4 date.

5 It's really what you were talking about
6 yesterday, Your Honor, where this is really asking the
7 question as a matter of fact whether something that is
8 disclosed within the four corners has certain properties,
9 and we know --

10 THE COURT: Yes, but let me stop. But the
11 difference when I talked about it is, at least as I
12 understood it, it's after the fact. Like as of today, is
13 the property inherent? That's a completely different
14 question than what was in the brain of a POSA when we look
15 at anticipation and obviousness.

16 So I don't -- I'm not buying into that, that
17 comparison respectfully, Mr. Gutman. I am --

18 MR. GUTMAN: Your Honor, may I try it another
19 way?

20 THE COURT: Yes.

21 MR. GUTMAN: The anticipatory reference itself
22 needs to be prior art.

23 THE COURT: Got that. I mean, anticipatory
24 reference is Pollyea. It doesn't sound like anybody
25 disputes -- actually, Ms. Bharkhda, do you dispute the

Swift - redirect

1 Pollyea 2009 prior art?

2 MS. BHARKHDA: The actual Pollyea 2009 article
3 that we just talked about entering, we do not dispute that.

4 THE COURT: Okay. All right.

5 MR. GUTMAN: And so, Your Honor, there are two
6 ways to anticipate it, expressly or inherently.

7 THE COURT: Right.

8 MR. GUTMAN: Dr. Swift is saying that Pollyea
9 2009 inherently discloses. So Pollyea needs to be prior
10 art, but the inherency part of it, the demonstration of what
11 is inherently disclosed within the prior art reference and
12 what you will rely on to prove what is inherent need not be
13 prior art.

14 THE COURT: I get that and I get, like, for
15 instance, you know, if it's inherent that, you know, a
16 structure has carbon atoms. Everybody knows that. I get
17 that. But what you seem to be doing is arguing that the
18 '444 patent, rather, Pollyea combined with the '444 patent
19 leads to these conclusions.

20 MR. GUTMAN: No.

21 THE COURT: That's where I'm losing you.

22 MR. GUTMAN: I apologize. If I led to your
23 misunderstanding, I apologize. We're not relying on the
24 '444 patent to demonstrate what's inherent in Pollyea. What
25 Dr. Swift was relying on were documents that matched up

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1 batch numbers.

2 THE COURT: I got that part. So now we're back
3 to then, why do you want to explore further this
4 relationship between the '444 patent and Pollyea? That's
5 where I lose you.

6 MR. GUTMAN: Because, you know, if plaintiffs
7 want to say they are not going to make a lack of enablement
8 argument for Pollyea, I don't need to ask these questions,
9 but, but Ms. Bharkhda asked questions to try to demonstrate
10 that Pollyea is not enabling for ibrutinib.

11 And so this isn't about the inherency part of
12 it. This is about the separate requirement that an
13 anticipatory reference must also enable what it discloses.
14 And so Ms. Bharkhda through her questions was trying to
15 establish that Pollyea is not enabled for what it discloses
16 and that's what my questions were addressing.

17 It's not, it's not addressing the inherency
18 question.

19 THE COURT: All right. Let me hear from Ms.
20 Bharkhda.

21 MS. BHARKHDA: Your Honor, in order for a
22 reference to be anticipatory, to anticipate, so for Pollyea
23 two anticipate claim 5 of the '444 patent, it not only has
24 to, it has to disclose the elements either expressly or
25 inherently.

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1 It also has to teach a POSA how to make and use
2 crystalline form A of ibrutinib with the five claimed peaks
3 of the '455 patent. So that's what it means when we say the
4 anticipatory reference has to be enabling.

5 THE COURT: Right. That makes sense. So that
6 makes sense to me.

7 MS. BHARKHDA: Okay.

8 THE COURT: So, now, there's probably maybe, you
9 know, a line here. Right? And in order for it to be
10 inherently enabling, the POSA would have to read it and
11 probably, would have to understand some concepts that are
12 not expressly set forth in Pollyea. You know, like, basic,
13 for instance, if I'm making a chemical, just turn the flame
14 on to heat the chemical or something like that. Right?

15 At some point you've got to bring in a POSA who
16 has knowledge that goes beyond the four corners of the
17 document.

18 Do you agree with that?

19 MS. BHARKHDA: Yes.

20 THE COURT: Where do you draw the line? By
21 going specifically to the '444 patent, it sounds to me like
22 obviousness. Where do you draw the line on that?

23 MS. BHARKHDA: If you are filling a hole in the
24 disclosure of the -- you are combining for the actual
25 teaching, you're in obviousnessland.

Swift - redirect

1 Now, you could potentially review the reference
2 to illustrate to the Court how a POSA would understand, for
3 example, terms or phrases that are used in the anticipatory
4 reference.

5 So, for example, in Pollyea, you know, it would
6 potentially be okay to look to a difference to explain to
7 the Court BTK, that a person of ordinary skill in the art in
8 2009 would have seen a reference to this term BTK and
9 understood that that was Bruton's tyrosine kinase. Maybe if
10 you go to a dictionary of tyrosine kinases or something like
11 that.

12 That is when it is okay to look outside the
13 extrinsic evidence, to explain how a POSA reading the
14 actual -- that they have in the anticipatory reference would
15 have understood those terms and phrases, but not being able
16 to fill a gap.

17 So I think when you are arguing that, when you
18 are combining the teachings of two difference, you are in
19 obviousness land.

20 I think here with this particular line of
21 questioning that Mr. Gutman is getting into that
22 precipitated my objection, the additional issue is Dr. Swift
23 never offered an opinion that if you look to the '444
24 patent, that would show that Pollyea would enable, would
25 meted the enablement requirement of an anticipation

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1 reference.

2 So the issue is Alvogen always had to prove that
3 Pollyea was an enabling anticipation reference, that it
4 would teach a POSA how to make and use claim 5, the elements
5 of claim 5, crystalline form A of ibrutinib with the six
6 claim peak. They always knew they had to do that. That's a
7 legal standard for anticipation.

8 They never offered an opinion for Dr. Swift
9 saying that she would combine Pollyea and the '444 patent in
10 order to show that it was enabling. That's the problem.

11 I mean, they are now trying to bring in another
12 reference to fill a deficiency. It was pointed out in
13 cross-examination. There wasn't any reason they couldn't
14 have disclosed that in her report because they always have
15 to show that. They always have to show that Pollyea is
16 enabling.

17 THE COURT: Okay.

18 MR. GUTMAN: Your Honor, we are not combining
19 references.

20 THE COURT: Well, we're past that. I kind of
21 did that, but I guess I'm still back now. It's not in the
22 report. Why should she be allowed to offer this opinion
23 right now?

24 MR. GUTMAN: Well, it's in response to the
25 cross-examination of Ms. Bharkhda. I mean, there was no

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1 testimony from Dr. Swift about the issues that we're
2 discussing right now on direct, so either --

3 THE COURT: But actually, the way she was
4 cross-examined was, my recollection was to show that if you
5 read the '444 patent, you could have figured out how to make
6 it. Right? No? All right. Hold on. Wait, wait. What
7 was the point -- Ms. Bharkhda?

8 MS. BHARKHDA: Actually, I think she was
9 questioned on cross-examination about the '444 patent not
10 disclosing any crystalline form of ibrutinib.

11 THE COURT: That's true. Okay. I do recall
12 that. All right.

13 MS. BHARKHDA: Yes.

14 THE COURT: So, Mr. Gutman, is that the limit of
15 the cross-examination? Now you want to bring in, she gets
16 what to say what about the '444 patent?

17 MR. GUTMAN: That the '444 patent teaches how to
18 make ibrutinib and one of ordinary skill in the art, at
19 least by the time that the '444 patent issued, would know
20 how to make ibrutinib, and therefore, that by itself
21 demonstrates that Pollyea that was published later and both
22 of them that were published before 2012, a POSA reading
23 Pollyea would know, there was public information, would know
24 how to make and use ibrutinib.

25 THE COURT: All right. Hold on one second. I'm

Swift - redirect

1 going to put you on mute one second.

2 MR. GUTMAN: Yes, Your Honor.

3 (Pause.)

4 THE COURT: All right. Here's where we were.

5 Ms. Bharkhda, I went off to speak with my law clerk who has
6 the same recollection I do.

7 I thought Dr. Swift actually testified
8 consistent with what I said, my recollection, that you could
9 have figured out how to make it from the '444 patent. You
10 don't think that she said that. I think the transcript,
11 it's obviously going to reflect what it will. I think she
12 has already testified to that.

13 MS. BHARKHDA: So I think I asked her whether it
14 disclosed any specific crystalline forms of ibrutinib. I
15 think she said, general conventional crystalline method and
16 general synthesis method for making ibrutinib or something
17 along those lines. Obviously, I have not read it in the
18 transcript.

19 But I think that was the nature of the
20 testimony. But she has not offered any opinion in the case
21 that somehow you would, the teachings of the '444 patent
22 would enable the Pollyea reference. That could have been
23 disclosed in her report.

24 MR. GUTMAN: This is extraordinary, Your Honor,
25 because the '444 patent is essentially the same '309

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1 compound patent that is being asserted against Alvogen and
2 if it's plaintiffs' position that the '444 patent doesn't
3 enable how to make and use ibrutinib, then the '309 patent
4 is invalid under 112.

5 MS. BHARKHDA: I mean, that's, Your Honor,
6 that's just a complete mischaracterization of both our
7 position and the line of questions Mr. Gutman was pursuing
8 with the witness.

9 THE COURT: Okay. I'm going to put you on mute
10 again.

11 All right. Here's what we're going to do. I'm
12 just going to let the testimony in. You can preserve the
13 objection and if we have to, we'll deal with it in
14 post-trial briefing. I don't want to delay further. I
15 really have a lot to learn, so now, keep in mind I've got a
16 12:00 o'clock proceeding and then another proceeding. They
17 are supposed to be quick so we can start at 12:30, but in
18 terms of timing, keep that in mind. So, Mr. Gutman, go
19 ahead.

20 MR. GUTMAN: Thank you, Your Honor.

21 BY MR. GUTMAN:

22 Q. Dr. Swift, is it your opinion that the '444 patent
23 would have taught one of ordinary skill in the art how to
24 make and use ibrutinib?

25 A. Yes, I think it would have.

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1 Q. I just want to go back to -- what was my last
2 question, actually. Can we go back to DTX-467, and I just
3 want to go down to the topics section.

4 I feel like we've addressed this, but I just
5 want to make sure, Dr. Swift. Did you rely at all on any of
6 this information in forming your opinions that Pollyea 2009
7 anticipates claim 5 of the '455 patent?

8 THE WITNESS: I specifically did not consider
9 that topic section because my instructions were to look at
10 material prior to 2012, and if I'm not certain that that
11 part of it is prior to 2012, my understanding is I was not
12 supposed to look at it. So I did not consider that part as
13 part of my decision.

14 MR. GUTMAN: Thank you, Dr. Swift. No further
15 questions, Your Honor.

16 THE COURT: All right. Thank you, Mr. Gutman.

17 Dr. Swift, I have a few questions for you. And
18 then I will let counsel for both sides if they have follow
19 up, ask. Sorry to subject you to further questioning.

20 What is PCI? API. If I said to you API, what
21 does that mean to you?

22 THE WITNESS: API is active pharmaceutical
23 ingredient.

24 THE COURT: Okay. PCI, does that mean something
25 to you?

Swift - redirect

1 THE WITNESS: My assumption was always that PCI
2 meant Pharmacyclics.

3 THE COURT: So it's not like in industry. You
4 don't look at PCI as an industry standard. It's not
5 something that the FDA looks at or anything like that. You
6 did not see PCI, come away with an understanding of an
7 industry term?

8 THE WITNESS: If it was, I was not aware of it.
9 That was not my assumption.

10 THE COURT: Okay. What's a poster board?

11 THE WITNESS: A poster board. When scientists
12 give presentations at meetings, you're either invited to
13 give an oral talk or you present a poster, which is what it
14 sounds like, usually a four-by-six large printed document --

15 THE COURT: Right.

16 THE WITNESS: That spells out the science and
17 then as other people come and visit you at your poster, you
18 describe what you did.

19 THE COURT: Okay. So when I look at the Pollyea
20 and it says, poster board, Roman Numeral III-649, what does
21 that mean?

22 THE WITNESS: So at the conference where this
23 poster was presented, there are typically lots of posters
24 presented at the same time and so the audience would walk
25 around to talk to whoever they wanted to speak to and

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1 there's typically a book of abstracts so that you can find
2 the person that you want to talk to.

3 So the posters would be arranged in the room
4 according to some number and that number just helps you find
5 the person that you want to talk to during the conference.

6 THE COURT: All right. And so that poster board
7 is literally the poster that's physically there; is that
8 right?

9 THE WITNESS: Yes.

10 THE COURT: And you say it's like a four-foot by
11 six-foot board? Is it going to have verbatim everything
12 that is in, for instance, if I were looking at a poster
13 board Roman Numeral III-649 of Pollyea, would the poster
14 board have every word of what is in what has been marked as
15 Exhibit DDX-467?

16 THE WITNESS: It would have that and more.
17 Typically, it would have more graphics. It expands upon
18 the --

19 THE COURT: Okay.

20 THE WITNESS: The subject that's summarized
21 here.

22 THE COURT: And I'm looking his Pollyea and it
23 says abstract. Right above poster board, it was abstract
24 3713 and above that, it says abstract. Right?

25 So what's an abstract?

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1 THE WITNESS: An abstract is a short nugget.
2 It's like a summary piece. You condense down your science
3 to try to attract an audience to come visit you.

4 THE COURT: Right.

5 THE WITNESS: So that's a summary piece.

6 THE COURT: And where I've seen abstract before
7 in the context of scientific things is, like, I see an
8 abstract of an article, which is a much lengthier exhibition
9 of topic. But can you have an abstract that just stands
10 alone, I take it?

11 THE WITNESS: You can. Typically, when my
12 posters, we have it, we might call it an abstract or we
13 might call it an introduction. That's the first little bit
14 of your poster and then it goes on.

15 THE COURT: So when I look at DTX-467, Pollyea,
16 is it an article, is it an abstract, is it a poster board,
17 what is it?

18 THE WITNESS: It's all of the above.

19 THE COURT: Okay. All right.

20 THE WITNESS: It is all of those things.

21 THE COURT: All right. Now, you said that when
22 you look at Pollyea, it wouldn't take much work to figure
23 out what the structure of PCI-32765 was.

24 Do you remember that?

25 THE WITNESS: Yes.

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1 THE COURT: All right. So what I want you to do
2 is, I want you to list as succinctly as you can what you
3 would have to look at beyond the four corners of Pollyea to
4 figure out, you know, what is the not too much work that had
5 to be done.

6 THE WITNESS: So I assume that you are familiar
7 with different types of search engines when you want to
8 look for literature. I could go on Google Scholar, for
9 example.

10 THE COURT: Let me put it this way. I'm a POSA
11 and I'm back in 2000, in early 2012. I've got Pollyea.
12 Right?

13 What am I going to do? When you say it wouldn't
14 take much work to figure out what the structure of PCI-32765
15 is. What's the not too much work I would have to do back in
16 early 2012?

17 THE WITNESS: Yes. So that not too much work
18 that I did. I literally typed into Google Scholar BTK, or
19 Bruton's tyrosine kinase inhibitor. That's what BTK stands
20 for. And I did a search and I constrained that search only
21 to articles and materials that would come up prior to 2012
22 and you get lots of hits. Lots of those hits say PCI-32765
23 in the title, and if you click on the first few, they take
24 you to articles that have the structure in them laid out for
25 you in the picture.

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1 THE COURT: Okay.

2 THE WITNESS: By them. If you do that search in
3 2020, you wind up with thousands of articles.

4 THE COURT: That's okay.

5 THE WITNESS: But if you constrain it 2012, you
6 still wind up with a hundred plus articles.

7 THE COURT: All right. I don't know if my
8 questions prompt any other questions from Mr. Gutman? No?

9 MR. GUTMAN: To the witness?

10 THE COURT: Yes. Right. To the witness.

11 MR. GUTMAN: Oh, yes. May I ask one question?

12 THE COURT: Look --

13 MR. GUTMAN: It is so brief.

14 THE COURT: No. Does it follow on what I asked?

15 MR. GUTMAN: It does.

16 THE COURT: All right. Go ahead and ask it.

17 BY MR. GUTMAN:

18 Q. Dr. Swift, does Honigberg 2010 relate PCI-32765 to the
19 structure of ibrutinib?

20 A. Yes. That's one of the articles that came up in the
21 search where PCI-32765 and the chemical structure are
22 identified together.

23 THE COURT: Okay. Ms. Bharkhda, do you have any
24 questions?

25 MS. BHARKHDA: I do not, Your Honor.

1 THE COURT: All right. Thank you very much.
2 Thank you very much, Dr. Swift. You're excused.

3 MR. GUTMAN: Thank you, Dr. Swift.

4 THE COURT: Okay. Counsel, let's see. Ms.
5 Clayton? Dr. Swift, you can leave. Okay?

6 (Witness excused.)

7 THE COURT: Yes? Ms. Clayton?

8 MS. CLAYTON: Your Honor, I was just getting
9 ready. We are going to break for lunch. The next witness I
10 believe is going to be Dr. Steed and he'll be ready after
11 lunch.

12 THE COURT: Is he your witness?

13 MS. CLAYTON: He's waiting. He's in the U.K.,
14 so it's starting to get a little late there. He was hoping
15 to go earlier, but he is available starting at 12:30.
16 Whenever the Court is ready.

17 THE COURT: We'll go as soon as I can. Did you
18 resolve the time issue?

19 MS. CLAYTON: Unfortunately, Your Honor, we have
20 not. Sandoz requested ten-and-a-half hours total of the
21 27 hours. I think by our calculations thus far, we've used
22 approximately an hour and 15 minutes and so we would ask to
23 have nine hours and 15 minutes more and my understanding is
24 that Alvogen is asking for less, or asking us to have less
25 because they have more patents.

1 We think obviously, we are not asking for half
2 because we realize they have more patents, but that gives
3 them 16 and a half hours and us ten-and-a-half and we think
4 that extra time gives them more than sufficient time to
5 cover all of their patents while making sure that we are not
6 prejudiced either.

7 THE COURT: Okay. Mr. Gutman, I've got to run,
8 but do you agree that's where we are, that you want 16 hours
9 and 15-minute of the total 27 hours? Is that right?

10 MR. GUTMAN: I'm not sure about the specific
11 break up, Your Honor. I apologize because I wasn't involved
12 in those negotiations.

13 THE COURT: Okay.

14 MR. GUTMAN: But I will say that, you know, we
15 have, Alvogen has two-thirds of this case in the defense as
16 opposed to Sandoz, which has one-third, and so --

17 THE COURT: And that's based on -- how do you
18 get the two third, one-third?

19 MR. GUTMAN: For example, Sandoz right now has
20 two witnesses that they want to direct and only two
21 witnesses that they want to cross, but we have many more
22 witnesses because we have many more claims and many more
23 patents.

24 And --

25 THE COURT: How many more claims do you have?

1 I've got to say we're confused here in the courtroom. I
2 didn't think there was a big difference in the number of
3 claims.

4 MR. GUTMAN: Well, I think, and, Ms. Clayton,
5 you can correct me if I'm wrong, but I believe that --

6 THE COURT: We have five and five. That's what
7 I'm told.

8 MR. GUTMAN: I don't know that that --

9 MS. CLAYTON: That's correct, Your Honor. The
10 one patent, the '604 patent, there are not going to be any
11 issues during trial, so there are three claims that we are
12 going to be presenting on.

13 THE COURT: All right.

14 MS. CLAYTON: Again, which is why we had said we
15 are willing to take less than half, ten-and-a-half total and
16 they can have 16 and a half.

17 THE COURT: You've got three claims. How many
18 claims do you have, Mr. Gutman?

19 MR. GUTMAN: Five, Your Honor, across four
20 different patents. The problem is also the claims that were
21 asserted against Alvogen were asserted in, you know, across
22 different patent families, so there's no easy way to address
23 those outside of addressing them individually.

24 And so one of the big issues here is that
25 Alvogen has to address four patents and Sandoz has to

1 address two patents, and that's creating some of the issue,
2 I believe, Your Honor.

3 THE COURT: I don't know. It sounds is pretty
4 reasonable to break it up, ten-and-a-half, 16-and-a-half.
5 I'm inclined to go with that. If you want to talk maybe
6 during lunch, but that sounds like a pretty reasonable
7 distribution of time.

8 So, all right. I've got to break for lunch.
9 We'll start at 12:30.

10 MR. GUTMAN: Your Honor, should I move the
11 exhibits into evidence?

12 THE COURT: We'll do it later on today, later on
13 in the day. Thank you.

14 MR. GUTMAN: All right.

15 (Luncheon recess taken.)

16 - - -

17 Afternoon session, 12:40 p.m.

18 THE COURT: All right. Good afternoon.

19 MR. SIPES: Good afternoon, Your Honor.

20 THE COURT: Apologies for the delay. One of the
21 conferences went late. Incidentally, the total time
22 yesterday, I'm going with defendant because it's a little
23 bit less total time to you all. I will give you the benefit
24 of that.

25 So plaintiffs used two hours and seven minutes.

Steed - direct

1 Defendants used five hours and 40 minutes. It was very
2 close to what we had, the total. All right?

3 MR. SIPES: Thank you, Your Honor.

4 THE COURT: Okay. Ms. Clayton, I guess you're
5 next?

6 MS. CLAYTON: Yes, Your Honor. At this time
7 Sandoz would call Dr. John Steed.

8 THE COURT: All right. Mr. Gutman, did you have
9 something that you needed to address? You're on mute.
10 Okay. He's go. We'll just go. Go ahead.

11 So actually, if I could have the witness raise
12 his right hand, please.

13 ... JONATHAN WILLIAM STEED, having been duly
14 sworn/affirmed as a witness, was examined and testified as
15 follows...

16 THE COURT: Counsel, you may proceed.

17 DIRECT EXAMINATION

18 BY MS. CLAYTON:

19 Q. Good afternoon, Dr. Steed.

20 A. Good afternoon.

21 Q. Can you tell us by whom are you currently employed?

22 A. Durham University in the U.K.

23 Q. What is your position at Durham University?

24 A. I'm a professor of medicinal chemistry.

25 Q. And if you could turn to DTX-1352 in your in your

Steed - direct

1 binder and if you could pull that up on your screen, what is
2 this document here?

3 A. This is my C.V.

4 Q. Does this C.V. adequately reflect your academic and
5 professional history?

6 A. It does.

7 Q. Okay. And have you created some slides today to help
8 aid in the presentation of your testimony?

9 A. I have.

10 Q. Okay. And if we could pull up the first of those
11 slides, DTX-6-3. Could you walk us through what you are
12 showing on this slide?

13 A. Yes. This is my academic and professional history in
14 brief. So I got my Bachelor's degree in chemistry from the
15 University College London, graduating in 1990 with first
16 class honors.

17 I got a Ph.D at the same institution in 1993.
18 Then post-doctoral for awhile and an academic position back
19 in London in 1995.

20 Since 2007, I've been a professor of chemistry
21 at Durham.

22 I'm Editor-in-Chief of the American Society
23 Journal Crystal Growth and Design, which as the name
24 suggests, is the American Chemical Society's journal in the
25 area of crystals.

Steed - direct

1 Prior to that I worked for the Royal Society of
2 Chemistry in the U.K.

3 Q. And as a professor, what type of classes do you teach?

4 A. I teach classes, chemistry. Particularly to do with
5 solids, materials, and techniques that are used to
6 characterize them as well as things like inorganic chemistry
7 and laboratory classes.

8 Q. When you say solid materials, does that include
9 crystals?

10 A. Yes, absolutely.

11 Q. Okay. And do you have a primary area of research that
12 you focus on?

13 A. Yes. My research is on solid forms of organic
14 molecules such as pharmaceuticals using crystallization
15 methodology and the way in which the solid forms are
16 characterized.

17 Q. And have you written or have you published articles in
18 peer-reviewed journals?

19 A. Yes. I'm the author of around 350 peer-reviewed
20 articles and international journals. Those articles have
21 been cited around 25,000 times.

22 Q. And have you published any books in the field of
23 crystals and crystalline form?

24 A. Yes. I'm an author of a book in 2000 called
25 Supramolecular Chemistry. It's the way in which molecules

Steed - direct

1 interact with each other. For example, the way they build
2 up crystals by joining one to another. That has been
3 translated into Russian and Chinese.

4 There was a second edition in 2009 and a third
5 edition will come out next year. So I regard it as the book
6 in the area. I've authored several books as well.

7 Q. So in total, how many years of experience do you have
8 in the study of crystals, crystalline form and associated
9 analytical testing?

10 A. Around 30.

11 Q. Okay.

12 MS. CLAYTON: Your Honor, at this time Sandoz
13 would like to tender Dr. Steed as an expert in the area of
14 crystal, crystalline forms and associated analytical
15 testing.

16 MR. SIPES: No objection, Your Honor.

17 THE COURT: All right.

18 BY MS. CLAYTON

19 Q. So before we get into the substance of your opinions,
20 I would like to give the Court an overview of what you are
21 going to walk through today.

22 If we could bring up the next slide, please.

23 And, Dr. Steed, can you tell us quickly the
24 areas of testimony you're going to walk through today?

25 A. Yes. I'm going to begin with a technology tutorial,

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1 crystals, I will touch upon claim construction and my
2 interpretation of a person of ordinary skill in the art.

3 And then I will be testifying towards the lack
4 of written description for asserted claims 18 and 19 in the
5 '548 patent and the resulting invalidity.

6 And then, finally, the lack of enablement of
7 asserted claims 18 and 19 of the '548 patent.

8 Q. Okay. And before we get into the tutorial, did you
9 reach an opinion in this case as to whether claims 18 and 19
10 are invalid for lack of written description or not?

11 A. I did reach an opinion. I believe they are invalid.

12 Q. Okay. And with respect to enablement, have you
13 reached a conclusion in this case as to whether claims 18
14 and 19 are invalid for lack of enablement?

15 A. I believe they are and not enabled.

16 Q. Okay. So before we get to the substance of those
17 opinions, let's talk about some of the technology at issue.

18 MS. CLAYTON: Your Honor, Dr. Swift talked about
19 some of these concepts yesterday, so if at any point you
20 feel like you already understand things and want us to move
21 along, just let me know. We're happy to do that.

22 THE COURT: Okay.

23 BY MS. CLAYTON

24 Q. Now, Dr. Steed, in general, what is a crystal?

25 A. So a crystal is a physical object. It's in this case,

Steed - direct

1 in the case of a pharmaceutical, it's made up of molecules
2 of that pharmaceutical extending effectively infinitely in a
3 three-dimensional space. And they have a periodic regular
4 repeating structure such that the crystal, the interaction,
5 made up of building blocks that repeat essentially.

6 Q. And if you could pull up the next slide, please,
7 DDX-6-5.

8 Dr. Steed, tell us what you're showing here?

9 A. Here I'm contrasting the crystalline solid with an
10 amorphous solid. In amorphous solid, the atoms or molecules
11 are arranged kind of randomly. An example of that might be
12 glass. Even though it's a hard transparent substance, glass
13 is actually amorphous. And that contrasts to a crystalline,
14 which is the subject matter we're talking about today, in
15 which the atoms or molecules have long range orders, so
16 there's a periodic and repeating array, like bricks in a
17 brick wall. An example might be diamonds.

18 Q. Okay. Now, you said that they have repeating
19 patterns. Do crystalline forms always have the same
20 repeating pattern?

21 A. No. The same atoms or molecules can adopt different
22 packing arrangements in the solid state and that gives rise
23 to different properties. We use the term polymorphism in
24 many shapes in the context of molecules, whether it's more
25 than one possibility of the range of the molecules.

Steed - direct

1 Q. Okay. If we could pull up the next slide. Dr. Steed,
2 could you tell us what you're trying to demonstrate through
3 these different arrangements here.

4 A. Yes. I think the brick wall analogy is quite helpful.
5 In this context I've taken a brick, which is represented
6 above the molecule or repeat unit of the crystal. I've
7 shown how that same brick can be arranged in many different
8 patterns, six possibilities are shown here.

9 And so a typical brick wall would be the
10 arranged form type of arrangement which gives it radial
11 strength as one brick overlaps with the joint between the
12 others. You can have them running stacked, joints running
13 up. Even the herringbone pattern you might find in a
14 driveway or something, more decorative. Made up of the same
15 fundamental block, the molecule, but it's repeating in a
16 different structure and that gives rise to the different
17 properties.

18 Q. Now, is there a common example of a substance that is
19 the same compound but exhibits different polymorphic or
20 crystalline forms?

21 A. Yes. The most easily appreciated is carbon, graphite
22 or diamond. It's not an exact analogy, but it gives you the
23 idea.

24 Q. And if you could pull up the next slide. And is that
25 what you are depicting here on this slide?

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1 A. Yes. That's right. So graphite and diamond are both
2 made up of arranged carbon atoms. The arrangement of those
3 carbon atoms is completely different between the two
4 materials. In diamond, each carbon atom which is
5 represented by black circles there is bonded to four
6 circles, kind of tetrahedrous sort of way, and that gives
7 rise to diamonds are hard materials as known.

8 Graphite is a different structure. Each carbon
9 is bonded, go with this sheet line structure. So graphite
10 is slippery. It is used as a lubricant, for example. Those
11 properties of graphite and diamond arrange from their
12 pattern arrangement.

13 Because carbon is a chemical element, and this
14 is called polymorphs, the idea is the same, that the
15 different structures give rise to different properties.

16 Q. All right. And so what about crystalline forms of
17 pharmaceutical ingredients? Do they exhibit different
18 physical properties if they have different crystalline
19 forms?

20 A. Yes. Each different crystal form of the
21 pharmaceutical has its own crystal pattern arrangement. You
22 can in turn determine its physical properties as a solid.
23 So, for example, different polymorphs will have different
24 stabilities, like chemical stabilities. There are different
25 solubilities and that impacts upon their bioavailability,

Steed - direct

1 how much actually gets into the bloodstream.

2 They'll have different crystal shapes sometimes
3 and that can create issues in terms of different polymorphs,
4 more or less formulated into tablets.

5 Q. Is it possible to distinguish one crystalline form
6 from another?

7 A. Yes. That is a very routine piece of technology. We
8 use various techniques, which we call characterization
9 techniques to identify characteristics of a particular
10 polymorph, but the most common is X-ray powder diffraction.

11 Q. Let's take a look at X-ray powder diffraction. And
12 can we bring up the next slide, please.

13 Dr. Steed, can you tell us using this slide how
14 X-ray powder diffraction works?

15 A. Yes. This is the basic geometry of an X-ray powder
16 diffraction experiment. So on the top left there we have a
17 source of X-ray. Literally live beams of X-rays at the
18 sample shown in the middle. In this context, our sample is
19 a powder, but a powder is made up of lots of different
20 crystals, so it's not amorphous, it is crystalline. Those
21 crystals are randomly oriented.

22 And the top, the powder sample, will diffract
23 into an X-ray beam in a variety of different directions.
24 I'm showing one them there. It is the scatter beam. And
25 the scatter beam is picked up by an X-ray detector which

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1 measures the intensity as a scattering angle. That is given
2 the name two $2\text{-}\Theta$, and I'm showing what it is, the angle
3 of the scattered beam compared to the straight beam.

4 Q. Now, when you run this in practice, is there only one
5 scattering beam that typically comes out of a scattering
6 sample?

7 A. No. When crystalline sample, it scatters the X-ray
8 beam in lots of different specific directions and the X-ray
9 detector is moved around the dotted circle there and it
10 measures the intensity in each particular value. So
11 some $2\text{-}\theta$ of values where there won't be any scattering,
12 no intensity other than background and some $2\text{-}\Theta$ values
13 will give rise to peak that arise from the scattering
14 sample.

15 Q. If we could pull up the next slide and are you showing
16 multiple scattering beams in this slide?

17 A. Yes. So each color barrier represents a different
18 scattering beam in cartoon fashion here. When these are
19 being hit with the sample, it scatters in a number of
20 different quite specific directions and the X-ray detector
21 makes its way around and measures the intensity of each
22 $2\text{-}\Theta$ point. From that we can work out where the
23 scattering beams, where they're heading.

24 Q. Okay. So I see the X-ray detector on the right. Tell
25 me how that is working in relation to the scattering beams

Steed - direct

1 and what is it doing?

2 A. Yes. So for each incident beam, a whole bunch of
3 scattering beams will come off. The X-ray detector makes
4 its way around the dotted line, around the circle and
5 measures the intensity of each angle and the high intensity
6 regions will be the scattering beam where there's no
7 intensity, where there isn't a scattered beam. The incident
8 beam can change as well.

9 Q. Does this result in a graph or plot of some sort?

10 A. Yes. The net result is a two-dimensional of the
11 intensity that the X-ray detector measures as a function of
12 that 2-Theta scattering angle.

13 Q. Okay. If we could bring up the next slide.

14 And tell us what you are showing here and how it
15 relates to the slide we just saw.

16 A. Yes. This is a relatively simple X-ray diffraction
17 pattern on the vertical axis. So what I've done is sort of
18 show how each of those colored beams coming off can be
19 mapped to a particular peak position. Some of those peaks
20 will be intense. The one labeled 100 is a very intense one.
21 You can see the sort of black bell-curved shape of a profile
22 with a peak there whereas some of the other peak positions
23 will have relatively low intensity and this overall pattern
24 of where the peaks are and their relative intensities acts
25 as a fingerprint for that particular crystalline form.

Steed - direct

1 Q. Okay. If we could pull up the next slide. You just
2 mentioned a fingerprint. So tell us how a fingerprint
3 relates to what we're seeing below.

4 A. Well, literally, just as an individual's fingerprints
5 are unique to them, can be used to identify them, so the
6 X-ray powder pattern diffraction patterns with their peaks
7 and relative intensity arise from the structure of the
8 crystal and can be used in a pattern recognition way to
9 identify which particular crystal form it is. So the
10 patterns are characteristic of a particular crystal form,
11 just like fingerprints are characteristic of a particular
12 individual.

13 Q. Now, looking at the graph that's on the bottom of that
14 slide, could you take a single peak and use it to identify
15 which crystalline form you have?

16 A. No, you couldn't. One peak cannot identify a
17 particular crystalline form. That's because multiple
18 different crystal forms may well happen to have a peak in
19 the same place. You can see from this, this is a typical
20 kind of powder diffraction for a small molecule on the drug
21 and you can see that particularly, a higher diffraction
22 angle above ten, there's also lots of peaks. So there's a
23 high chance of one or more of those peaks might happen to be
24 in the same place in more than one polymorph. So you have
25 to look at the whole pattern and match the whole pattern

Steed - direct

1 with a reference standard in order to identify a polymorph.

2 Q. And is that similar to a fingerprint in any way?

3 A. Yes. Exactly. You wouldn't identify a person by
4 looking at just one ridge of their fingerprint, reading a
5 couple ridges. You look at the whole print and compare it
6 to a reference or what you might have on file for them.

7 Q. Now, did your brick analogy also help you explain why
8 you can't use one or even two peaks to identify a specific
9 crystalline form?

10 A. Yes, it does, I suppose.

11 Q. Okay. Bring up the next slide. Yes.

12 A. Yes. So the actual, the actual position and intensity
13 of a peak is a complex result of the way literally the
14 electrons are distributed in the crystal, and by electrons,
15 I just mean the position of the molecules. The molecules
16 have electrons in them.

17 And so this is not really a direct map to any
18 particular structure of the molecule that is in the crystal.
19 What I've done here is just for the sake of highlight, I've
20 highlighted a particular motif within the crystal. There
21 are two bricks at 90 degrees to one another.

22 And even though the three that I've highlighted,
23 for that matter, the herringbone, too, all have this
24 particular feature in them, imagine that correlates to a
25 peak on the simplest graph.

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1 Then these three have the same kind of feature.
2 They are all quite different pattern arrangements, different
3 polymorphs, so there's a fair chance that two different
4 polymorphs might have a similar feature in them and give,
5 that would give rise to a similar X-ray diffraction peak,
6 but they're definitely different.

7 Q. So if two crystalline forms share the same peaks, what
8 does that tell us about the similarity between the two
9 crystalline form?

10 A. Nothing, really. It's just coincidence. Somewhere in
11 the middle of the crystals somewhere there is some electron
12 that happens to be similarly spaced. Essentially, it
13 doesn't tell us anything about the crystals. Just
14 coincidence.

15 Q. If they share two of the same peaks, does it tell us
16 they share the same crystalline structure in any way?

17 A. No. It's the whole pattern that derives from the
18 structure. There's information about the structure in all
19 of these. You can't really single out one peak and
20 correlate it with a structure.

21 Q. Okay. Now, you say you can't use 1 or 2 peaks. Is
22 there a number of peaks at which point if those two forms
23 have it in common, you could say, okay, they have enough
24 peaks in common, they are likely the same crystalline form?

25 A. Yes. The best practice is to use the whole

Steed - direct

1 diffraction pattern as a fingerprint. The United States
2 Pharmacopeia suggests that a technical person who is trying
3 to compare them to a reference standard, it is sufficient
4 from the USP's view to stand for the ten strongest peaks.
5 Then you have a pretty high chance you've identified a
6 particular example against a reference of the ten strongest
7 peaks you can match up. Even that's just a shorthand for
8 the whole pattern.

9 Q. If we could pull up JTX-0322, Dr. Steed, what is this
10 document?

11 A. As I mentioned, the United States Pharmacopeia. This
12 is, this is the outer cover of the 2012 edition, edition 35.

13 This has become a national repository of
14 standards for pharmaceuticals within the U.S. and this
15 gives, this gives standard methodologies, for example, for
16 analyzing. So this document that I was quoting suggests the
17 ten strongest peaks are a good approximation for the whole
18 pattern.

19 Q. Okay. If we could turn to pages 430 to 431 of this
20 document and if we could call out on the right-hand side the
21 bottom paragraph that starts with qualitative. And we see
22 the highlighted section on the right.

23 Is that the language that you were referring to
24 with respect to the USP?

25 A. That's right. This is the section of the United

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1 States Pharmacopeia, Chapter 941, that teaches a person of
2 skill how to identify a sample that they have in their
3 possession against a requisite standard by means of X-ray
4 powder diffraction.

5 You can see in the highlighted, generally
6 identified in a single X-ray. So you take your reference
7 standard with the ten strongest peaks and compare that to
8 your unknown. If they match, you can consider yourself to
9 have identified that particular crystal form.

10 MS. CLAYTON: Your Honor, I think Covington
11 might need to mute themselves.

12 THE COURT: Okay. Did they do it?

13 MS. CLAYTON: Thank you.

14 BY MS. CLAYTON

15 Q. So let's say that you've run a sample and you have a
16 pattern. What do you do next? What do you do with that
17 pattern?

18 A. So the question is what polymorph is that -- does that
19 pattern correspond to and when a polymorph is discovered, it
20 will be studied and a reference, reference pattern will be
21 published and perhaps in assign particular paper, perhaps in
22 an electronic database and so the known crystal forms that
23 will be available somewhere in the literature, a reference
24 standard pattern.

25 You can go and compare the one you just made

Steed - direct

1 with, as I say, ten strongest peaks or ideally the whole
2 pattern matches up. Of course, if you can't find anything
3 that it matches in the published literature in electronic
4 databases, you may have made a new form.

5 Q. Okay. So can we pull up the next slide. Is this
6 showing one of the, the type of comparison that you just
7 mentioned?

8 A. Yes. So this is taken from my report and in this
9 case, I was over laying the X-ray powder diffraction pattern
10 with form I shown in red of ibrutinib with the pattern of
11 form A shown in the '548 patent. I'm showing this because
12 you can see whether the pattern peak positions and relative
13 intensities matches up.

14 So in this case, there's a mismatch here in the
15 two different patterns. You can see that quite easily by
16 over laying the two patterns.

17 Q. Okay. So we just discussed what crystalline forms
18 are, some of the techniques used to analyze them. I want to
19 now turn to how we actually make these crystals. And let's
20 turn to the next slide, please. And tell us what you are
21 trying to demonstrate through this slide.

22 A. Yes. So there are lots and lots of different ways to
23 make a crystal and new ways are being invented on a
24 continual basis. That's part of my research. But perhaps
25 the most common way is to use a solution-based approach and

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1 there are two ways you can do that, evaporation shown on
2 this slide or cooling.

3 And very, very simply, it's supposed to be a
4 simple process to do evaporative crystallization. You
5 simply dissolve your compound of interest. You get a powder
6 in a liquid called solvent in which it's soluble. It might
7 be water. It might be sugar in your tea for example, or it
8 might be some other organic liquid. It dissolves.

9 We've got to bring an increase in the
10 concentration of the molecules in that solution to the point
11 where they are no longer soluble and the way we do that in
12 an evaporative process, we just let it evaporate, so the
13 liquid passes from liquid to the vapor phase. There's less
14 liquid and that concentrates the sample.

15 And so here's a point where the crystals are no
16 longer soluble and they begin to crystallize out. One of
17 the solvent evaporated crystals should be present at the
18 bottom and side of the vial. You can dry the crystals.

19 Q. And is there also a process similar to this, but it's
20 called a cooling process?

21 A. Yes, that's right.

22 Q. Okay. And if we could pull up the next slide. So
23 describe for us how the cooling process works as opposed to
24 the evaporation process.

25 A. Yes. And I stress again, there are many ways to make

Steed - direct

1 crystals, but these kind of solution-based approaches are
2 perhaps the most popular. This is a very similar idea.
3 Again, we're going to dissolve solids and the powdered
4 sample in a solution.

5 Another idea here is that the compound is more
6 soluble when the solution is hot than when it's cold and
7 that's very, very common. I heat it. There's a name there
8 going up the solution. You dissolve as much as you can
9 while it's hot and then as the solution is allowed to cool,
10 perhaps by leaving it in the ambient atmosphere, then the
11 solubility of the compound would decrease and, again,
12 crystals should begin to form.

13 And once those crystals are formed, once the
14 solution is cooled to room temperature, for example, you can
15 use filtration to obtain the solid characterization.

16 Q. Okay. Now, are these the only two crystalline,
17 crystallization techniques that can be used to make
18 crystalline form?

19 A. No, not by a long way and these are being developed
20 all the time. So, for example, we could also use melting of
21 the solid. We can use grinding. We can use some
22 advancement, such as non-compliant crystallization
23 technologies. We can use, there are diffusion techniques.
24 So the whole range of different techniques, some of them
25 very common.

Steed - direct

1 Q. Okay. Now, in these two processes that we just looked
2 at, the evaporation and cooling process, are there different
3 variables that are involved here that can affect the
4 crystalline form that you obtain?

5 A. Yes. The particular crystalline form, polymorphic
6 form that comes from any crystallization is a function of
7 the exact conditions on which the crystals grow. And so
8 even within these relatively simple to do, but a one off
9 solution based crystallizations. One is a solvent.

10 There are probably hundreds of different
11 solvents you can use of which certainly many have common
12 usage. You can change things like cooling rates, the
13 heating rate, the temperature, the concentration, things
14 like the conventional flow within the vials. Stirred or not
15 stirred. The list is quite long.

16 Q. Let's just pull up the next slide.

17 You talked about solvent and crystallization
18 potentially giving different methods. What about these
19 other items that are listed on this slide? Can those
20 variables affect which crystal form you obtain?

21 A. Yes. All of these are more counter effects of crystal
22 form because the crystal forming, the exact circumstances
23 under which the nucleus form, the molecules begin to form
24 together to form the first beginnings of the crystal. And
25 each of these particular sets of conditions or variables can

Steed - direct

1 affect that.

2 Crystallization method I described in the
3 solvent. I think I didn't mention pH. That can make a
4 difference as well. Even the dry conditions. When the
5 sample is moist, it may be one form. When it is dry, it may
6 transport to another.

7 Q. Okay. Now, do we see examples in the '548 patent of
8 how some of these different variables can affect the
9 crystalline form that you obtain?

10 A. Yes, we do.

11 Q. Okay. If we could pull up JTX-1, which is the '548
12 patent. And I'd like to start by looking at column 64,
13 which is Example 1.

14 So, Dr. Steed, what does Example 1 of the '548
15 patent talk about?

16 A. Example 1 is quite a long example, and this is where
17 the inventors of the patent give us the recipes by which, by
18 which a person of skill could make and reproduce each of the
19 six crystal forms that are disclosed in this patent. So for
20 each crystal form, there is one or more recipes that if you
21 follow them carefully, then you should end up making the
22 disclosed crystal.

23 Q. Okay. And if we could go to column 66 here and I want
24 to specifically highlight the paragraph where it says form D
25 and form E.

Steed - direct

1 Now, what solvent is used to make form D?

2 A. That's a solvent called MIBK, a common solvent.

3 Q. And what solvent is used to make form E?

4 A. That's totally a different solvent.

5 Q. Right. And so is it fair to say that the use of those
6 two different solvents give you two different forms of
7 ibrutinib?

8 A. Yes. They are different forms of ibrutinib and
9 clearly, they're coming from different solvents. They just
10 go straight to the point, different solvents can result in
11 different crystalline forms.

12 Q. All right. Now let's go to column 65, form A through
13 three, and column 66, which discusses form C.

14 Now, form A, route three and form C, what
15 solvent are both of these examples using?

16 A. Both of these use methanol points. There's no
17 difference of solvents in this case.

18 Q. So why are we getting different forms even though the
19 same solvent is used?

20 A. A long story short, it's the details of all the other
21 things that have changed in the crystallization. So, for
22 example, you can see that the solutions are heated to
23 different initial temperatures, 45 versus 50 degrees.
24 There's a different concentration of ibrutinib within the
25 methanol. In Form A, 3, it's 12 grams in 120 mLs, which is

Steed - direct

1 a different ratio of two rounds and 25 mills. There are
2 various differences. But, again, it shows you it's not just
3 solvents. There are other differences within the details of
4 the recipes that give rise to the different crystalline
5 forms.

6 Q. Are these groups that we're looking at here and shown
7 in Example 1, are these the cooling and evaporation
8 crystallization processes that you were talking about
9 earlier?

10 A. Yes, that's right. These are solution-based
11 crystallization methods.

12 Q. And I think you said solution-based crystallization
13 methods are common and known to those in the art; is that
14 right?

15 A. Yes.

16 Q. All right. Is it, even though those are common, is it
17 common and routine to vary all the variables we just
18 discussed to be able to arrive at every crystalline form of
19 a compound?

20 A. Not every crystalline form, no. It is common and
21 routine to do what's called a polymorph screening. So
22 that's where when you have a new active ingredient and
23 you've got a molecule, you can do these kinds of
24 experiments. You can vary some of the conditions fairly
25 exhaustive and try to find the most stable form. That's a

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1 very different kind of inquiry to try to find every single
2 possible form of a given compound. I think we still don't
3 know how to do that.

4 You would never be sure if you're finished.
5 There could always be a form yet.

6 Q. Okay. Now, in advance of -- let's say you have form
7 A, Route 3, but you have not discovered form C yet.

8 Would you know that making the changes to the
9 form A route 3 would result in form C before you conducted
10 the experiment?

11 A. No, not at all. You can never know -- without trying,
12 you can never know what set of conditions will give rise to
13 a particular polymorphic form. So the way to proceed is
14 just to try different sets of conditions, different
15 crystallization methods, and see what results in analyzing
16 crystals.

17 So given the teachings to make form A with a
18 recipe shown on the left here, the only thing you would know
19 is you must do something else, but you wouldn't know what,
20 what, if anything, would give rise to anything new. You
21 just have to keep trying things until you find something
22 different or until you run out of resources or time or
23 interest.

24 THE COURT: Doctor, can I -- if I could, if you
25 could, if you could slow down a little bit, we would

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1 appreciate it over here.

2 THE WITNESS: I apologize, Your Honor.

3 THE COURT: Don't apologize. Just it helps.

4 Thanks.

5 BY MS. CLAYTON

6 Q. Now, before you actually make a given crystalline
7 form, do you know in advance what physical properties that
8 form will have?

9 A. No. You have to make a measurement, long story short.

10 Q. Okay. So what type of techniques would you run then
11 to see what crystalline form you have?

12 A. Yes. In terms of identifying crystal form, X-ray
13 powder diffraction. I talked about earlier, it's probably
14 the most common, most useful, because the X-ray powder
15 diffraction is a fingerprint for that particular crystalline
16 form. And there are other characterization techniques as
17 well, but do provide some bits of useful information.

18 Q. And can you predict in advance what that pattern will
19 look like for a particular crystalline form?

20 A. Typically, there are some advanced computation
21 approaches that can generate hundreds or thousands of
22 possible crystal forms, but you don't remember which of
23 those will come out of a particular set of conditions and
24 what the properties will be without actually trying.

25 Q. Okay. Now, with that background, I would like to turn

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1 to some of your opinions in this case. Let's bring up the
2 outline of his testimony again at 16-17.

3 And so next let's turn to your definition of a
4 person of ordinary skill in the art. Have you, do you have
5 an opinion on what the definition is for a person of
6 ordinary skill in the art in this case?

7 A. Yes, I do.

8 Q. And if we could pull up the next slide.

9 Does this summarize the experience that you
10 think a person ever ordinary skill in the art should have
11 for the '548 patent?

12 A. Yes, it does. A person of ordinary skill is a pretty
13 highly skilled kind of person that's educated to at least
14 degree level, if not Ph.D. level, and have experience in
15 crystallization of the kind we talked about as well as
16 characterizing solid forms and then also be family with the
17 beginnings of formulation, pre-formulation, testing that
18 goes with it.

19 Q. Okay. And are you aware of the definition of a person
20 of ordinary skill that plaintiffs' expert, Dr. Myerson, has
21 offered in this case?

22 A. Yes, I have.

23 Q. Okay. If we could bring up the next slide. Does this
24 slide reflect the summary of your understanding of Dr.
25 Myerson's definition of a person of ordinary skill?

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1 A. Yes, it does.

2 Q. Is your definition and Dr. Myerson's definition the
3 same or different?

4 A. They are different in some regards. For example, Dr.
5 Myerson places less stress on the knowledge of a medicinal
6 chemistry, saying just some knowledge is required.
7 Generally, that's similar in terms of the kinds of skill
8 that we both think a person of skill would possess.

9 Q. Okay. And so do your opinions in this case turn on
10 whether the Court adopts your definition of a person of
11 ordinary skill and Dr. Myerson's definition?

12 A. No, they don't.

13 Q. Okay. Now, let's move on to claim construction. Are
14 you aware whether there was a claim construction order
15 issued in this case for the '548 patent?

16 A. Yes, I believe there was.

17 Q. Okay. If we could pull up demonstrative 6-20.

18 Does this reflect the claim construction
19 definition that you understand the Court issued in this
20 case?

21 A. Yes, that's my understanding.

22 Q. And for a crystalline form of ibrutinib, what claim
23 interpretation are you applying for that phrase, a
24 crystalline form of ibrutinib?

25 A. Well, I based my opinion of invalidity through the

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1 lens of plaintiffs' interpretation of claim construction.

2 In other words, that this phrase, a crystalline form of
3 ibrutinib is not limited to forms A through F, but could
4 refer to any possible form of crystalline form of ibrutinib
5 whether known at the time of the filing of the '548 patent
6 or not. Indeed, whether known now or not.

7 Q. All right. And one last housekeeping question that I
8 forgot. Do you qualify as a person of order skill in the
9 art under your definition and Dr. Myerson's definition?

10 A. Yes, I believe so.

11 Q. Okay. Now let's turn to your invalidity analysis.
12 And I would like to review the legal standard that you were
13 instructed to apply in this case. If we could pull up
14 DTX-6-22.

15 And so, Dr. Steed, I know you're not a lawyer,
16 but could you explain in your own words for us what do you
17 understand you were supposed to look at in conducting your
18 written description analysis?

19 A. Yes. As you say, I'm not a lawyer, but I guess the
20 instruction I was given is shown on the slide 3.

21 My basic understanding of written description,
22 that the inventors have to show by means of what they write
23 in the disclosure that they're in possession of the full
24 scope of the invention, that they actually had what they
25 claimed they would invent and they have to establish that,

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1 so a person of skill would have that description.

2 Q. Okay. And what about this last bullet point about if
3 the patent claim covers a genus? I know it's a complicated
4 concept, but what is your layman's understanding of the
5 genus standard in the context of written description?

6 A. Yes. Insofar as a genus is appropriate, in other
7 words, a group of inventions with something in common that
8 allow them to become grouped together, then it's my
9 understanding there has to be a representative number of
10 examples so that a person could recognize what it is that
11 this genus has in common and separate it from things that
12 aren't part of the genus or a series of features, the
13 structure, members of the genus, again, that a person can
14 recognize and understand what that genus is.

15 Q. Okay. So let's start your analysis by looking at the
16 claims of the '548 patent. If we could pull up JTX-1 again.
17 And let's start with the cover page, please.

18 And so, Dr. Steed, what is the title of the '548
19 patent?

20 A. It's called crystalline forms of ibrutinib tyrosine
21 kinase inhibitor.

22 Q. And what is, what Bruton kinase inhibitor is this
23 invention specifically referring to?

24 A. That means ibrutinib.

25 Q. Okay. And who are the inventors on the '548 patent?

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1 A. Norbert Purro, Mark Smyth, Erick Goldman and David D.
2 Wirth.

3 Q. Okay. And so now if we could go to column 80 and pull
4 up claims 15 through 19 of the '548 patent.

5 And so what are the claims that are at issue
6 here in this litigation?

7 A. It's my understanding just claims 18 and 19.

8 Q. Okay. And in your understanding, based on plaintiffs'
9 interpretation, what is the scope of claim 18 of the '548
10 patent?

11 A. So my understanding is that this is an extremely broad
12 claim, so any, any crystalline form of ibrutinib, whether
13 known at the time of the filing of the patent or not,
14 indeed, whether it's discovered now or not, a peak of
15 18.9 degrees and unsolvated would fall under this claim
16 under plaintiffs' interpretation of the Court's claim
17 construction.

18 Q. And 18.9 2-theta feature, did that come from
19 independent claim 15?

20 A. Yes, it does.

21 Q. All right. And what about claim 19? Based on
22 plaintiffs' interpretation, what does claim 19 of the '548
23 patent cover?

24 A. That will be very similar. It's claim 18 and the
25 limitation, depending as it does from claim 16, that there

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1 should also be a peak at 16.1 degrees.

2 Q. Okay. And how do claims 18 and 19 of the '548 patent
3 compare to the original claims that were filed in connection
4 with the '548 patent application?

5 A. They're very, very different. Much, much broader.

6 Q. Okay. If we could pull up JTX-41. If we could zoom
7 in on that cover page, please.

8 Dr. Steed, what is this document?

9 A. This is the file wrapper of the '548 patent.

10 Q. Okay. And if we could turn to Bates ending in 1484.

11 MS. CLAYTON: Your Honor, for the record, this
12 is one of those really voluminous exhibits and we've only
13 provided an excerpt for the Court.

14 THE COURT: Okay. Thank you.

15 MS. CLAYTON: Sorry. Bates ending '386 first,
16 Your Honor. I jumped ahead.

17 BY MS. CLAYTON

18 Q. So, Dr. Steed, what is this portion of the file
19 history?

20 A. So I understand this is the patent application that
21 eventually became the '548 patent as it was originally
22 filed.

23 Q. Okay. And if you would turn -- this document is
24 slightly out of order the way the Patent Office kept it.
25 Could you turn two pages earlier, please, which is ending in

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1 1484.

2 And what is this portion of the file history
3 showing us?

4 A. So these are the original claims as the inventors
5 originally filed them.

6 Q. Okay. And what were these claims and the original
7 claims directed to?

8 A. There's one independent claim, claim 1, and that's
9 directed specifically to just one crystalline form,
10 crystalline form A of ibrutinib characterized by 3 2-Theta
11 peaks in the positions listed. The other 12 claims are all
12 dependent on claim 1.

13 Q. Now, to the best of your understanding, what happened
14 to these original claims?

15 A. To my understanding, the inventors cancelled these 13
16 claims that were directed just to crystalline form A.

17 Q. Okay. If we could turn to a later portion of the file
18 history ending in Bates number 1519.

19 And what do you understand this document in the
20 file history to be?

21 A. So this is --

22 THE COURT: Wait. Stop. Sorry. I want to find
23 it. Okay. Go ahead. Thank you.

24 BY MS. CLAYTON

25 Q. All right.

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1 A. So I understand this is an amendment to the
2 application in which they amended their claims during the
3 process of the prosecution of the patent.

4 Q. Okay. And if we could turn the page ending in Bates
5 number 1422. And, Dr. Steed, what was this document dated?

6 A. April the 4th, 2018.

7 Q. Okay. And who is it signed by?

8 A. It's signed by Jana A. Lewis.

9 Q. Okay. If you could turn now, just a couple pages
10 later to Bates ending, one-page later, 1523.

11 And what is this page reflecting?

12 A. So these are the now amended claims beginning with the
13 amended claims.

14 Q. Okay. And what does it show happened to claims 1
15 through 13?

16 A. They were canceled.

17 Q. Okay. And if we could go down to claim 44 of this
18 amendment, please, which is on the next page ending in Bates
19 number 1524.

20 Does claim 44 match up with claim 15 of the '548
21 patent?

22 A. Yes, it does.

23 Q. Okay. Have you created a slide that shows how these
24 new claims match up with claims 15, 16, 18 and 19 of the
25 '548 patent?

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1 A. Yes, I have.

2 Q. If we could pull up demonstrative, defendants'
3 demonstrative 6-23.

4 So what is this demonstrative showing here, Dr.
5 Steed?

6 A. Yes. Well, here I'm just mapping all of the new
7 claims from that amended claim listing that we were just
8 looking at. What's at issue is the '548 patent. Just
9 as we saw in the previous slide, the new claim 44 maps to
10 what became claim 15 of the '548 patent, and similarly,
11 new claims 45, 48 and 49 now map to claims 16, 18 and 19,
12 which, of course, the last two are the two that are at
13 issue.

14 Q. Okay. Now, speaking about the issued claims here and
15 talking about them for a moment, are you aware that
16 plaintiffs claimed these claims, in fact, all of them, cover
17 a genus of crystalline forms of ibrutinib?

18 A. I've heard that argument.

19 Q. Do you think that makes sense in the context of what
20 these claims, or how these claims read?

21 A. No I don't at all. I don't really understand how you
22 can describe crystalline forms. Each crystalline form is
23 unique. It has its own unique crystal pattern arrangement
24 formed by a different method. In each case as we've seen.
25 And with its own unique set of properties.

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1 So I can understand the concept of the genus as
2 it might apply to a chemical molecule, for example. So a
3 chemical molecule might have a particular fragment on it,
4 and as a synthetic chemist, I might know how to add benzene
5 rings to a variety of different molecules if they had some
6 useful properties, for example, and then I could recognize a
7 genus of chemical molecules with benzene rings on them.

8 I never have to make that and I can recognize it
9 by looking at that genus. The crystalline forms are all
10 unique. Each one is unique and unto its own rights. So
11 trying to group them into a genus doesn't make any sense to
12 me.

13 Q. Could you describe I want you to create a crystalline
14 form that has a peak at 18.9, but you could with a chemical
15 compound that has a benzene ring?

16 A. No. It's completely different. There's no way to
17 control where the peaks are. So the information of the
18 peaks is determined by the very complex sort of series of
19 interactions between molecules of the crystals formed and
20 effectively, I don't want to add more, but effectively, the
21 crystal by virtue of its, the pattern arrangement that it
22 falls into, then generated its own powder diffraction
23 pattern, which we can't predict without doing the experiment
24 in advance and seeing what form actually comes out.

25 So there would be nothing about having in my

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1 possession one compound that makes another polymorph, 18.9,
2 where they could do that with a chemical compound to install
3 fragments of molecules.

4 Q. Okay. Now, let's turn to actually the actual
5 disclosures in the specification of the '548 patent.

6 THE COURT: Actually, can you just give me a
7 second. Thanks.

8 MS. CLAYTON: Sure.

9 THE COURT: All right. Ms. Clayton, this is
10 what makes it very difficult with the zoom compounded by I'm
11 sure the distance that we are from London or England and
12 mastering accents as well.

13 I think this is a pretty important part of the
14 testimony. You had asked a question something along the
15 lines of, could you describe I want you to create a
16 crystalline form that has a peak at 18.9. It's a little
17 garbled to us. But you could with a chemical compound that
18 has a benzene ring. And then there was an answer.

19 I would like you, if you could, just to repeat
20 that question and we can have the professor respond again,
21 just so I would like to make sure the record is very clear
22 on this point.

23 MS. CLAYTON: Yes.

24 THE COURT: Do you know what I'm talking about?

25 MS. CLAYTON: I am. I'm going to pull up my

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1 real time to make sure I remember which specific question.
2 It doesn't sound like it's exactly what I asked. I think if
3 I take a look at it --

4 THE COURT: If you are looking at real time,
5 it's literally the first line on the page and it follows
6 testimony that trying to group them into a genus doesn't
7 make any sense to me.

8 MS. CLAYTON: Okay. Okay. Yes.

9 THE COURT: All right. So if we could just
10 begin. And I don't think it's -- it's not bad if we have to
11 repeat it. That's fine. I think it's important to get this
12 very clear. Thank you.

13 MS. CLAYTON: Okay.

14 BY MS. CLAYTON

15 Q. You described how you would be able to add a benzene
16 ring to a chemical compound. Is it possible to
17 intentionally add a 2-Theta peak at 18.9 to a crystalline
18 form?

19 A. No, it isn't. Long story short, nothing about, even
20 if I had in my possession another crystalline form that had
21 a peak at that position, there's nothing about that that
22 would tell me how to add peaks at that position. I was
23 explaining, trying to do it a little bit more slowly, that
24 the position of the peaks, the whole pattern arises from,
25 from the detailed distribution of the molecules within the

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1 crystal, and that's not something that we can control as
2 chemists.

3 We just have to bring about a situation in which
4 crystals will form all by themselves and whether they do
5 that, the result is a crystal which gives rise to a
6 diffraction pattern, and you get what you are given. You
7 can't control that process. So you would have no idea
8 whether it's going to be a peak at any particular 2-Theta
9 position until you went and measured it, having completed
10 the crystallization process.

11 MS. CLAYTON: Is that clear, Your Honor?

12 THE COURT: That's clear to me. Thank you.

13 MS. CLAYTON: Okay.

14 THE COURT: Basically, Doctor, there's no
15 predictive ability here essentially that you can, is the way
16 to think about it?

17 THE WITNESS: Exactly, Your Honor, yes. Just do
18 the crystallization, see what you get.

19 THE COURT: All right.

20 BY MS. CLAYTON

21 Q. Now, let's turn to the disclosures in the '548 patent
22 itself. Which crystalline forms of ibrutinib does the
23 specification in the '548 actually describe?

24 A. It describes six crystalline forms. Forms A, B, C, D,
25 E and F.

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1 Q. And what type of position does the specification
2 provide for the six specific forms?

3 A. It provides a lot of information. It describes how to
4 make them. That's what we looked at. At least one recipe
5 for each crystal form. And then it describes how to
6 recognize them. So there's at least an X-ray powder
7 diffraction pattern for each of these six crystal forms
8 given in the patent. And there's also most of the
9 crystalline forms, there's other kinds of information as
10 well. Characterization techniques such as DSC, TGA,
11 infrared spectroscopy and things like melting point and
12 stability as well.

13 Q. Okay. So you say it teaches how to make them. Let's
14 take a look at that. If we could go back to Example 1 of
15 the '548 patent, column 64 through 66. Again, is Example 1
16 the example that teaches you how to make crystalline form
17 2-Theta?

18 A. Yes. These are the recipes that get you these six
19 forms.

20 Q. How many recipes does it provide for form A?

21 A. There are three variations, all of which end up making
22 Form A.

23 Q. What about for form B?

24 A. Two for form B.

25 Q. And what about for each of forms C, D, E and F?

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1 A. One each for each of those.

2 Q. Okay. Now, does the '548 patent describe how to make
3 any crystalline form of ibrutinib besides the six forms we
4 see here?

5 A. No, not at all. These recipes are each directed
6 specifically to ending up with these six forms.

7 Q. Okay. Now, does the '548 patent, I think you said it
8 provides the X-ray powder diffraction pattern for each of
9 these six forms. Is that right?

10 A. Yes, it does.

11 Q. All right. If you would pull up the next slide. What
12 are you showing on this slide?

13 A. Yes. So here I've just extracted from the patent's
14 disclosure each of the six X-ray powder diffraction
15 patterns. There are only six of them. They are all shown
16 here. There's one given as a representative
17 characterization for each of the six forms of the patent
18 actually disclose it. So forms A through F.

19 Q. And so for the record, that's figures 1, 5, 9, 12, 14
20 and 16 in the '548 patent?

21 A. Correct.

22 Q. Okay. Now, are there any other X-ray powder
23 diffraction patterns in the '548 patent besides the six we
24 see here?

25 A. No, just these 6, 1 for each of the forms that's

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1 disclosed.

2 Q. Okay. And I think you said that there are some other
3 physical properties for each of these forms that are
4 described in the '548 patent. Did I state that correctly?

5 A. Yes, that's correct. It's a characterization of
6 processes.

7 Q. Okay. Let's take a look at just one example of that
8 and if we could go to Column 2, lines 50 through Column 3,
9 line 15 of the '548 patent. What are we seeing in this call
10 out?

11 A. This is a listing of all the information that's
12 provided for crystalline form A. So we can see, for
13 example, sort of bullet point A there, the X-ray powder
14 diffraction pattern in Figure 1. Some characteristic peaks
15 are called out in peak B there, stability. Certainly,
16 humidity. And then the patent goes on to say it's providing
17 us with the infrared spectrum, which characterizes the way
18 the molecule vibrates. Can also be indicative of a solid
19 form. It provides the DSC thermogram. That's the
20 differential scanning calorimetry. That measures the
21 thermal behavior of samples. Heat it up. Whether it's
22 going to melt or change form or any other behavior like
23 that, which is again characteristic of a particular
24 crystalline form.

25 We're also told that we get the

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1 thermogravimetric analysis. That tells you whether a sample
2 loses weight. If it was a solvate, you would expect it to
3 lose weight.

4 And then it talks about the positions of the DSC
5 thermogram, activity correlating to a melting point and.
6 Something about its solubility.

7 Q. Now, is similar information provided for the other
8 crystalline forms in the specification, namely, form B, C,
9 D, E and F?

10 A. Yes. They're similar kinds of information, at least
11 the powder X-ray pattern. Typically, DSC and other
12 information at this time.

13 Q. Okay. Now, is this physical information provided for
14 any crystalline form of ibrutinib besides forms A through F?

15 A. No, no, not at all. All information relates to forms
16 A through F, nothing else.

17 Q. Okay. Now, I want to take a look at a few other
18 portions of the specification and if we could pull up three
19 portions together. The abstract, the field of the
20 invention, and column one, line 26 through 33, which is a
21 summary of the invention.

22 Now, here in the abstract, do you see where it
23 says described here in is the BTK inhibitor and gives the
24 name of ibrutinib, including crystalline form solvate and
25 pharmaceutically acceptable salts? Do you see that

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1 language?

2 A. Yes.

3 Q. Do you see similar language in the field of the
4 invention?

5 A. Yes.

6 Q. Okay. Now, does this language that says, including
7 crystalline form, does that tell you as a person of ordinary
8 skill in the art that the inventors were in possession of
9 crystalline forms of ibrutinib besides A through F in any
10 way?

11 A. No, no, not at all. This is just general introductory
12 text that tells a person reading it that they are going to
13 be reading about crystalline forms of ibrutinib. I take
14 that to mean some crystalline forms, the ones that are then
15 later described, not all crystalline forms.

16 Q. All right. And what about that text there in the
17 summary of the invention where it says, described
18 herein is ibrutinib, including solvates, hydrates,
19 polymorphs.

20 Does that tell a person of skill like
21 yourself that the inventors possessed forms other than A
22 through F?

23 A. No, not at all. Again, this is very, very general
24 introductory text that just says what I'm going to read
25 about when I read the invention. There can be some

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1 pharmaceutically acceptable solvates, polymorphs, so on.

2 Q. Okay. If we could look a little further down in
3 Column 2 of the '548 patent, lines 13 through 16. And do
4 you see hear it says, also described here in are methods for
5 preparing crystalline forms of ibrutinib?

6 A. Yes, I see that.

7 Q. Does having this general language that describes here
8 our method for preparing crystalline forms of ibrutinib,
9 does that tell you that the inventors had methods of making
10 forms other than A through F?

11 A. No. Again, this is very general introductory text.
12 It just says the patent is going to be describing some
13 methods for preparing some crystalline forms of ibrutinib,
14 the ones that the inventors actually knew how to prepare.
15 It doesn't tell you anything else about anything in them.

16 Q. If we could turn further in the patent at column 79,
17 lines 8 through 11. And it's right above the claims. And
18 hear it says, the examples and embodiments described here in
19 are illustrative and various modifications or changes
20 suggested to persons of skill in the art are to be included
21 within the disclosure.

22 Now, does this language suggest to you that the
23 inventors were in possession and had identified crystalline
24 forms to size A through F?

25 A. No, not at all. I think this language is referring to

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1 the fact there's more than one way to skin a cat. So, in
2 other words, there are, for example, three ways given to get
3 to form A. It's form A in every case, but you can make it
4 by some variations of a big crystallization methodology, and
5 that's quite common.

6 There are lots of different ways of
7 crystallizing it and getting to form A and that's what the
8 inventors are including here. I wouldn't be able to claim I
9 had anything new if I just ran a slightly different
10 crystallization method and got that form A.

11 Q. So looking at the specification as a whole, in your
12 opinion, does the specification inform you as a person of
13 skill in the art that the inventor could actually have
14 invented any crystalline form other than A through F as of
15 the filing date June 4, 2012?

16 A. No. It's quite clear that this is directed specific
17 to crystalline forms, ways to make them.

18 Q. Okay. If, in fact, they had discovered other
19 crystalline forms and had invented them as of June 4th,
20 2012, what type of information would you expect to see in
21 the specification of the '548 patent?

22 A. Similar to the information that was provided in the
23 six forms the inventors do disclose, you would expect at the
24 very least a way to make any other crystalline forms,
25 crystallization method, at least one and a way to recognize

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1 those crystalline forms. At least x-ray powder diffraction
2 pattern.

3 I fully expect based on documents like this
4 other information to be provided as well. Particularly
5 things like stability and so on so that a person would know
6 how the form is to be used or what it's for.

7 Q. Okay. So, Dr. Steed, we've just gone through the
8 specification and I want to talk about how those disclosures
9 match up with the claims here.

10 So what is your understanding as to which
11 crystalline forms that Dr. Myerson says are disclosed in the
12 '548 patent and match up with claim 18?

13 A. So I believe there's just two forms, form A and C.

14 Q. And that's because those are the two forms that have a
15 2-Theta peak at 18.9, 16.1 and are unsolvated? Is that an
16 accurate statement?

17 A. For claim 18, I think they just need the 18.9 peak.

18 Q. You're correct. It was not an accurate statement. So
19 let me re-ask that question. So for the reason that --
20 well, why don't you tell me. What is the reason that forms
21 A and C match up with claim 18?

22 A. Yes. So forms A and C both have peaks of 18.9. They
23 are both crystalline forms of ibrutinib and they are both
24 non-solvates.

25 Q. Okay. And what about for claim 19? Which of the

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1 forms discussed in the '548 patent match up with what's
2 required for claim 19?

3 A. Now we've introduced another peak at 16.1 and that is
4 just form A.

5 Q. Okay. So we've been talking about the disclosures in
6 the '548 patent and the claims and I want to talk about the
7 forms that you understand the plaintiffs actually
8 discovered.

9 So which forms of ibrutinib do you understand
10 that Pharmacyclics had actually discovered as of June 4th,
11 2012?

12 A. It's the same. My understanding is that they had
13 discovered forms A through F.

14 Q. And what is that understanding based on?

15 A. Well, that's the testimony of the inventors themselves
16 and it's also repeated in Dr. Myerson's expert report.

17 Q. As of today, are there crystalline forms of ibrutinib
18 besides A through F that are known to exist?

19 A. Yes, yes. Many new forms have been discovered since
20 the filing of the '548 patent. I think we're up to about 20
21 forms now.

22 Q. Have you created a chart that shows the forms that
23 you're aware of that not just to claims 15 through 19?

24 A. Yes, I have.

25 Q. Okay. If you could pull that up. So, Dr. Steed, what

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1 are we seeing here?

2 A. So this is the basis of a non-comprehensive literature
3 search. As far as I'm aware, these are the, these are the
4 list of crystalline forms that have been published,
5 discovered since the filing of the '548 patent. They
6 weren't known at that time that would fall under the claims
7 of the '548 patent.

8 Q. All right. And so for claim 15, which requires a
9 crystalline form of ibrutinib with a peak at 18.9, how many
10 different forms of ibrutinib have been discovered after
11 June 4, 2012, that have a peak at that position?

12 A. At least the eight listed here, perhaps more.

13 Q. Okay. And what about crystalline forms with peaks at
14 18.9 and 16.1? How many crystalline forms have been
15 discovered since for this chart, June 4th, 2012, with peaks
16 at those positions?

17 A. Yes. At least three additional forms.

18 Q. Okay. And what about for forms that have a peak at
19 18.9 and are unsolvated as required by claim 18? How many
20 forms are you aware of that have been discovered since
21 June 4th, 2012?

22 A. At least two more forms that are listed there.

23 Q. And the same for claim 19. How many forms that match
24 claim 19 are you aware of that have been discovered since
25 June 4th, 2012?

Steed - direct

1 A. At least one, one more.

2 Q. Okay. Now, I want to take a closer look at a couple
3 of these, but first let's look at them altogether.

4 Can we pull up the next slide, which is
5 demonstrative 26. And what are we showing on this slide?

6 A. This is just the front page of different patents or
7 patent applications that have disclosed the forms I was
8 listing on the previous slide.

9 Q. Okay. And just for the record, this includes JTX-34,
10 which is the '802 patent; JTX-57, which is the '468
11 patent; JTX-57, which is the '468 patent; JTX-31, which is
12 the '869 patent; JTX-68, which is the EP842; and JTX-56,
13 which is the '026 patent.

14 Dr. Steed, now, are the inventors that are
15 listed on these patents, are they the same as the inventors
16 that are on the face of the '548 patent?

17 A. No. They are all different. These forms were
18 invented by different inventors.

19 Q. Okay. Now, let's take a closer look at the '889
20 patent, which is JTX-13. Now, if we could zoom in on that
21 patent.

22 Dr. Steed, when was this patent filed?

23 A. November 26, 2014.

24 Q. Okay. And how many years after the filing of the '548
25 patent was that?

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1 A. It was about two-and-a-half years.

2 Q. Okay. And what is the title of this patent?

3 A. It's crystalline form I of ibrutinib.

4 Q. Okay. If we could go to Examples 1 and two of this
5 patent, which is in column four.

6 Dr. Steed, what do Examples 1 and 2 of the '889
7 patent describe?

8 A. These are two alternative recipes by which the
9 inventors of the '889 patent are telling you how to make
10 their invention, which is crystalline form I of ibrutinib.

11 Q. Okay. And what solvent combination do they use?

12 A. It is a mixed solvent. It's a mixture of 2-propanol
13 n-heptane.

14 Q. Okay. And is this mixture of solvent described in any
15 of the recipes that we saw in the '548 patent in Example 1?

16 A. No.

17 Q. Okay. And I quickly want to go back to the '548
18 patent, too, Example 1. Column 64 and look at the form A,
19 Route 1.

20 So we see four lines down, isopropyl alcohol is
21 mentioned.

22 Do you see that?

23 A. Yes.

24 Q. Is isopropyl alcohol the same thing as 2-propanol?

25 A. It is.

Steed - direct

1 Q. Now, is using 2-propanol as a single solvent in a
2 crystallization route the same thing as using 2-propanol and
3 n-heptane as a solvent mixture?

4 A. No, it isn't. A mixture of solvents will have its own
5 properties and effectively act as if it were a new solvent
6 with its own range of properties. Of course, we're taught
7 by the '548 patent that using isopropyl alcohol alone gives
8 us form A and so clearly, there was something different
9 about the isopropyl alcohol and n-heptane mixture that's
10 giving form I.

11 Q. Okay. If we could turn to form A, route two in column
12 65. Do you see in the second line down it says heptane?

13 A. Yes.

14 Q. Now, is the solvent heptane the same as the solvent
15 n-heptane?

16 A. No, it isn't. The heptane refers to a kind of a
17 low rate mixture of a bunch of different types of heptanes.
18 It may include some n-heptane, but not all heptane mixtures.

19 Q. And is using the heptanes as a solvent the same as
20 using a mixture of 2-propanol n-heptane?

21 A. No. Of course, we're taught that heptane in this
22 context gives us form A. Of course, the mixture 2-propanol
23 and n-heptane give us form I.

24 Q. Okay. If we could go back to JTX-13, which is the
25 '889 patent. Does the '889 patent provide an X-ray powder

Steed - direct

1 diffraction pattern for form I?

2 A. Yes.

3 Q. If we could pull up Figure 1 of the '889 patent. And,
4 Dr. Steed, is this X-ray powder diffraction pattern of the
5 '889 patent for form I?

6 A. Yes.

7 Q. How does this pattern compare to the X-ray powder
8 diffraction pattern for A through F in the '548 patent?

9 A. It's a different pattern. Different intensities,
10 different peak positions. It clearly identifies form I as a
11 different crystalline form polymorph to forms A, B, C, D, E
12 or F.

13 Q. Have you overlaid this diffraction pattern with the
14 patterns in the '548 patent?

15 A. Yes. I've looked at each one carefully using the kind
16 of overlay I showed earlier.

17 Q. Okay. If we could pull up PTX-6-27. And does this
18 show those over lays?

19 A. Yes, it does. So in blue here, I've got that X-ray
20 diffraction pattern, which is looking at the '889 patent.
21 Just using the PowerPoint, I've lined up the 2-Theta scales
22 so that they are directly comparable and I've overlaid in
23 blue the with each of these six patents for A, B, C, D, and
24 E and F and looked at them in detail peak by peak and the
25 overall appearance of the patent and assured myself that

Steed - direct

1 form I is a different form to any of the other forms A
2 through F in the '548 patent.

3 Q. Okay. Now, what form of ibrutinib do you understand
4 that Sandoz uses in an ANDA product?

5 A. They use form I.

6 Q. And does Sandoz's ANDA also include X-ray powder
7 diffraction pattern data for form I?

8 A. It does.

9 Q. And did you also do a comparison of that X-ray powder
10 diffraction data for form I with the X-ray powder
11 diffraction pattern for A through F in the '548 patent?

12 A. Yes, I did.

13 Q. If we could pull up the slide DDX-6-28. And for the
14 record, these are pulled from DTX-2232.

15 Dr. Steed, can you describe for us what we're
16 seeing here?

17 A. Yes. This is in my report and it's the same kind of
18 an exercise. So, again, we've got in black the X-ray powder
19 patents for form A through F of the '548 patent.

20 At this time I overlaid the X-ray powder
21 diffraction patent, sample form. I again carried out that
22 comparison with the whole patent, detailed overlay. You can
23 see in more detail that form I in Sandoz's hands is also
24 different to each of the forms A through F.

25 Q. Okay. How, are you aware that Dr. Myerson argues that

Steed - direct

1 Sandoz's form I uses the teaching of the '548 patent and a
2 method in which it's arrived at?

3 A. I've heard of that.

4 Q. Do you agree with that?

5 A. No, I don't.

6 Q. All right.

7 MS. CLAYTON: Your Honor, at this time we need
8 to show a document from our supplier and the supplier
9 produced it and made available with strict instructions that
10 only certain parties can access it, so we would ask to seal
11 the courtroom at this time for a brief portion of Dr.
12 Steed's testimony.

13 THE COURT: Well, I don't know how we seal the
14 remote courtroom. I mean, I can tell you that visually, my
15 understanding is that the only people who are participating
16 visually are the parties and the Court, but there is access
17 to the proceedings by audio only by the public at large and
18 I have no way of knowing if there's anybody present from the
19 public. Hold on.

20 MS. CLAYTON: Your Honor, this is a public
21 dial-in that is active. There are also several individuals
22 in the room who we're not entirely certain who they are.
23 The only people that they could be are either clients or
24 approved by the parties because the parties and the Court
25 are the only ones who were given links.

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1 THE COURT: Okay. That's right. And like, for
2 instance, there's my law clerks half on occasion linked in,
3 whatever, if that is what the right word would be. I don't
4 know, Ms. Clayton. How do you want to handle it?

5 MS. CLAYTON: I don't know if it would be
6 possible to keep just us, the Court, the witness and
7 plaintiffs' counsel here. If there's a dial-in, we can't
8 close that off and it may not be possible. I just have to
9 make sure that, you know, I have lodged that request with
10 the Court, Your Honor.

11 THE COURT: Well, you've lodged the request with
12 the Court, but I can't -- hold on.

13 I mean, Saji, can you put us in a private room
14 such that the particular information is not shared with the
15 public call in?

16 TRIAL TECH: Yes. If you give me a couple
17 minutes, I can push everyone out who isn't one of the
18 parties or the Court into a waiting room.

19 THE COURT: Okay. We can try that. You say a
20 few minutes. We could take a break then if you want.

21 MS. CLAYTON: Sure. That works. And, Saji, our
22 clients, my client hasn't been able to see this information.
23 The client requested that it literally be the lawyers, the
24 expert and the Court.

25 TRIAL TECH: Are there other witnesses you would

Steed - direct

1 like to push out as well?

2 MS. CLAYTON: Yes, Your Honor.

3 TRIAL TECH: Great. I just need a couple
4 minutes.

5 THE COURT: All right. So then --

6 MR. SIPES: Your Honor, I want to bring up one
7 quick thing. Mr. Sipes for plaintiffs.

8 THE COURT: Yes.

9 MR. SIPES: I think one of our experts may be
10 zoom in, that's the verb I will use. Dr. Myerson, who will
11 be responding to Dr. Steed, it would be helpful to keep him
12 zoomed in, too, if it's possible to identify him.

13 MS. CLAYTON: That's perfectly fine, Your Honor.

14 THE COURT: Okay. So, Saji, is that possible?

15 TRIAL TECH: That's fine. Is that Alan Myerson?

16 MR. SIPES: That's correct.

17 TRIAL TECH: Great. I will keep him in.

18 THE COURT: Okay.

19 MR. SIPES: Thank you.

20 THE COURT: And then, Saji, how much time would
21 you like? Ten minutes, 15 minutes, what do you mean?

22 TRIAL TECH: Maybe like two minutes.

23 THE COURT: Then, parties, do you want to take a
24 15-minute break now? You tell me. Ms. Clayton, what are
25 you thinking?

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1 MS. CLAYTON: I'm good with maybe just a short
2 break, Your Honor, under five minutes.

3 THE COURT: Okay. Then we'll go for five
4 minutes. We'll be back at 2:10. Thanks.

5 MS. CLAYTON: Thanks.

6 (Short recess taken.)

7 - - -

8 MS. CLAYTON: Just let me know when you are
9 ready, Your Honor.

10 THE COURT: I am ready.

11 MS. CLAYTON: Okay.

12 BY MS. CLAYTON

13 Q. If we could pull up JTX-0573 and if we could call up
14 the top part of the document and then the bottom part of the
15 document as well together.

16 Dr. Steed, what is this document?

17 A. This is a section of the Drug Master File from
18 Sandoz's supplier that describes the manufacturing process
19 of ibrutinib.

20 Q. Okay. And if we could turn to the second page of this
21 document and zoom in on that.

22 What is this page showing?

23 A. Yes. So this is a pretty complex looking chemical
24 diagram. This is a kind of chemical flow chart showing
25 the individual chemical reaction steps that are involved

Steed - direct

1 in, first of all, building the ibrutinib molecule, and then
2 subsequently the crystallization steps that result in form
3 I.

4 So everything all the way up to the bottom row,
5 second molecule from the left are chemical steps in which
6 the molecules are being transformed one into the other and
7 we don't actually get to the molecule ibrutinib until the
8 second structure on the bottom row from the left.

9 Q. Could we highlight that structure to make it clear
10 what -- can we highlight that second structure? When you
11 say the second structure on the bottom, is the highlighted
12 one the one you're referring to?

13 A. That's right. That's the ibrutinib molecule, so
14 that's being made in that step.

15 Q. Okay.

16 A. As it's labeled there.

17 Q. Okay. So the first time we see ibrutinib, it's
18 labeled ibrutinib form E.

19 Do you see that?

20 A. Yes.

21 Q. And then it looks like it gets transformed to
22 ibrutinib form C? Is that correct?

23 A. Correct.

24 Q. And then what happens next?

25 A. And then it's re-crystallized and it forms form I,

Steed - direct

1 which is the form that Sandoz actually used.

2 Q. Are you aware that Dr. Myerson contends that because
3 forms E and form C are intermediate that are formed
4 during the manufacture of form I, this somehow means that
5 the teachings of the '548 patent are used in arriving at
6 form I?

7 A. I've heard that, that theory, but I don't agree with
8 it.

9 Q. Well, why do you not agree with that theory?

10 A. What's happening here is that the ibrutinib molecule
11 happens to be made in toluene in that last chemical
12 synthesis, step five, and so when they isolate the ibrutinib
13 solid for the first time, it just happens to come out in
14 solvate because the chemistry is done in toluene. That
15 happens to be what's in the '548 patent, form E. They
16 dissolve that solid up to get rid of the toluene and the
17 toluene solvate and that first, that crystallization step
18 and purification step is step six. That involves methanol.
19 And then we get a solvent in freeform, form C. Sandoz still
20 doesn't want form C, so they use this ethanol water step to
21 recrystallize again to get form I. At each stage --

22 THE COURT: So, Doctor, Dr. I think you've got
23 to slow down again.

24 BY MS. CLAYTON

25 Q. Doctor, let me ask you a question. So you have

Steed - direct

1 ibrutinib form E and then it looks like you're going to
2 dissolve it in methanol. What happens to the crystal
3 structure of form E when you dissolve it and heat it up?

4 A. All the crystals dissolve, so all information, all
5 traces of that crystal structure is gone because you're
6 forming a solution in the ways that we described earlier.
7 And so, in fact, all you end up with during the process of
8 step six is a methanol solution of ibrutinib. And so it
9 actually wouldn't matter what form ibrutinib you started
10 with.

11 Q. And so what about then when you get to form C and you
12 dissolve it in ethanol and water? What happens to the
13 ibrutinib form C once it gets dissolved?

14 A. This is another solution crystallization process we
15 were describing earlier and again you end up with a solution
16 of ibrutinib in ethanol and water which then crystallizes
17 form I. Again, it wouldn't matter what form you started
18 with. It's the crystallizing of ethanol and water that's
19 important and that gives you form I.

20 Q. Okay. Now, is there any disclosure in the '548 patent
21 of starting with form C and then using ethanol in water to
22 convert it to form I?

23 A. No, not at all.

24 Q. And, again, is there any information related to the
25 physical properties of form I anywhere in the specification

Steed - direct

1 of the '548 patent?

2 A. No.

3 Q. Okay.

4 TRIAL TECH: I'm sorry to interrupt. I've
5 just gotten an e-mail asking if I can permit Dominick
6 Gattuso, who is counsel for Sandoz?

7 MS. CLAYTON: We are actually done with this
8 line of questioning.

9 THE COURT: Wait. Before you go, hold up.

10 MS. CLAYTON: Yes.

11 THE COURT: Hold up.

12 MS. CLAYTON: But Mr. Gattuso can come in.

13 THE COURT: You can bring in Mr. Gattuso. All
14 right. Just hold on a second.

15 Just in terms of going forward, there's going to
16 have to be cross-examination on this point. I guess we'll
17 have to break out another room for cross-examination. In
18 terms of drafting an opinion or speaking about something,
19 I've got to think about how to do it.

20 So basically, you're saying that it confidential
21 that during the manufacturing process they make ibrutinib
22 form E and ibrutinib form C. Right? I mean, that's a fair
23 summary of what they do to make this API. Correct?

24 MS. CLAYTON: Correct. The supplier designated
25 this document highly confidential. Your Honor, it is

Steed - direct

1 possible, depending on what cross is, that we might be able
2 to substitute this version with one that has a lesser
3 confidentiality designation on it if that would be helpful
4 for purposes of the record.

5 THE COURT: I think the least that goes under
6 the seal is always the better. We really should try to
7 avoid that.

8 MS. CLAYTON: Yes.

9 THE COURT: And so, for instance, if it's really
10 not a big secret that the manufacturing process by the
11 supplier makes ibrutinib form E, then ibrutinib form C, you
12 know --

13 MS. CLAYTON: Sandoz has a document with this
14 same schematic. It's not this full document, so we could, I
15 guess, substitute. If there aren't questions asked about
16 the later portion of the document, we could substitute this
17 version for that version.

18 THE COURT: This is not a secret. It could be
19 made public?

20 MS. CLAYTON: Yes. This portion, yes.

21 THE COURT: Oh, okay. All right.

22 MR. SIPES: Your Honor, actually, I have a
23 question about that. I will need to be mindful of this on
24 cross. So if I come either to the name of the third-party
25 supplier or -- can you hear me?

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1 THE COURT: Yes.

2 MR. SIPES: The name of the third party supplier
3 for this particular synthetic group, do I need to ask for
4 the courtroom to be closed or not? That's what I'm trying
5 to figure out.

6 MS. CLAYTON: So with respect to just the
7 synthetic route and the name, that is fine.

8 MR. SIPES: Okay.

9 MS. CLAYTON: Until you get to later portions of
10 the document.

11 MS. SIPES: That's very helpful.

12 THE COURT: Okay.

13 MR. SIPES: And, Your Honor, we'll try to do,
14 all the testimony and we're done with the trial and we've
15 had a couple of days to sleep, try to come up with an
16 agreement in the trial transcript what would be the part
17 that needs to be sealed for purposes of making the writing
18 of an opinion easier. So we'll try to resolve that
19 question, too, when the record is closed and we can look at
20 what's in the record, to minimize what is sealed.

21 THE COURT: I think to date, there's nothing.

22 MS. CLAYTON: I agree with that, Your Honor.

23 THE COURT: Okay.

24 MR. SIPES: If my understanding from Ms. Clayton
25 is correct, that what we've been talking about doesn't have

Steed - direct

1 to be sealed, that's my understanding.

2 THE COURT: Okay. Great. Thank you for both
3 being helpful.

4 All right. Saji, you can take us all back out.

5 MS. CLAYTON: Can we pull that down?

6 THE COURT: We can proceed now. Thank you.

7 BY MS. CLAYTON

8 Q. Now, I want to turn back to slide, the slide with the
9 new forms that have been created. I think it's slide 25.
10 Okay.

11 Now, have you looked at the disclosure of each
12 of these patents?

13 A. Yes, I have.

14 Q. Okay. And have you created a chart that summarizes
15 some of the information that is in those patents?

16 A. Yes, I have.

17 Q. Okay. If we could pull up demonstrative 6-29.

18 Now, what are we seeing here in this chart?

19 A. Yes. So these are the, that listing of
20 later-discovered forms. So I've just listed where they are
21 published, when that patent application was filed, the route
22 of crystallization of these later discovered forms and the
23 X-ray powder diffraction pattern, whether or not it's
24 different to the X-ray powder diffraction patterns disclosed
25 in the '548 patent. And these are the other forms -- forms

Steed - direct

1 that I -- that we're talking about.

2 And so where I've written different there, that
3 means under my analysis, each of these forms have a
4 different X-ray powder diffraction pattern to any of the six
5 forms and their X-ray powder diffraction pattern disclosed
6 in the '548 patent.

7 Q. All right. And so are the route of and
8 crystallizations described here, are those disclosed in the
9 '548 patent?

10 A. No, not at all of these are all different recipes that
11 of course result in different forms.

12 Q. What about the X-ray powder diffraction for each of
13 these patterns? Does it match up with any of the X-ray
14 powder diffraction patterns shown in the '548 patent?

15 A. No. They're all different. These are all different
16 to the six forms that are reported in the '548 patent.

17 Q. Okay. And if we could go back to slide 25 again.

18 So, Dr. Steed, I want to focus on claims 18 and
19 19 that are listed here for a moment. And are you aware
20 that plaintiffs and Dr. Myerson contend that the universe
21 and genus of crystalline forms described by claim 18 is
22 narrow because only two new forms are listed in this chart?

23 A. I've heard that argument.

24 Q. Do you agree with that argument?

25 A. No, I don't, just because --

Steed - direct

1 Q. And why is that?

2 A. Sorry. Just because we happen to have already found
3 two additional forms in addition to the two that are
4 disclosed in the '548 patent that fall under claim 18 don't
5 in any way limit the universe of forms that are covered by
6 claim 18. There could always be more forms discovered if
7 new crystallization method are invented or new
8 crystallization methods to try.

9 Even though we only know of two additional forms
10 in addition to what the '548 patent disclosed, there could
11 be unlimited number of forms disclosed, discovered in the
12 future as crystallization technology advances. So it's
13 still an unlimited universe even though we only know of two
14 forms so far.

15 Q. What about 19? Do you agree with Dr. Myerson's,
16 plaintiffs' argument, that the scope of claim 19 is narrowed
17 because to date you're only aware of one additional form
18 that meets the claim limitation?

19 A. I'm aware of an argument, but I don't agree with it.

20 Q. And why is that?

21 A. Well, again, let me put it this way. Already in less
22 than ten years, we found another form that falls under claim
23 9 that the inventors weren't in possession of and, again,
24 this is an unlimited universe.

25 At any point another crystallization method

Steed - direct

1 could be developed and another crystallization technique
2 could be tried that result in yet another form that happens
3 to have two peaks in this crowded region in the 18.9 and
4 16.1 region and that could go on without limit.

5 Q. In fact, have you worked on compounds where new
6 crystalline forms have continued to be discovered for years
7 after the original forms have been discovered?

8 A. Yes. Part of my research is inventing new ways to
9 produce crystalline forms and, yes, I've worked on an
10 example. It's a drug precursor to the anti-schizophrenia
11 drug Galantamine, where there are 14 forms, of which three
12 of them have been discovered in 2019 and 2020.

13 Q. What is the name of that compound?

14 A. We called it ROY. The polymorphs happen to have a
15 very attractive red, orange and yellow color, so we called
16 it ROY for short.

17 Q. If we could pull up DTX-1308, please. And, Dr. Steed,
18 what is this document?

19 A. This is a pre-print of a paper that I'm a co-author
20 on. It was developed this year. This is the
21 pre-publication version. Developed a new crystallization
22 method.

23 MR. SIPES: Objection, Your Honor. I don't
24 believe this is in his report. If it is, I apologize. I
25 don't recall seeing this in his report.

Steed - direct

1 MS. CLAYTON: It's in his reply report at
2 paragraph 58, Your Honor. It's on Page 19. It's the last
3 article listed there, Tyler.

4 MR. SIPES: Your Honor, all I was going to say,
5 if that's a paper, that's fine. There's no except from it.
6 There's no indication that he's going to talk about anything
7 about the contents of the paper.

8 If he's going to talk about what's in the text
9 of his report, that's fine, but there's no indication from
10 this that he's going to at all get into anything else that
11 is in the paper. And it's sort of interesting the way it
12 has been cited, you can't even tell that Dr. Steed is an
13 author.

14 MS. CLAYTON: Your Honor, all he's going to
15 establish is to show the article is concerned within that
16 method.

17 THE COURT: Yes. I'm going to overrule the
18 objection. I mean, we don't need to go into much. The
19 point here is that they continued to develop crystalline
20 forms. Right?

21 MS. CLAYTON: Correct, Your Honor.

22 THE COURT: He has made that point. I get it
23 and he personally has and it's reflected in this article.

24 Is there anything else you need to dive into on
25 this particular study?

Steed - direct

1 MS. CLAYTON: No, Your Honor.

2 THE COURT: All right. Then I'm going to
3 overrule the objection.

4 MR. SIPES: Thank you, Your Honor.

5 BY MS. CLAYTON

6 Q. All right. And if we could pull up DTX-1307. And is
7 this another article about the ROY molecule that you cite in
8 your report?

9 A. Yes, it is.

10 Q. And does this article also discuss a new form of ROY
11 that has been discovered recently?

12 A. Yes. This article was published just last year in
13 Montreal. They also mentioned a new crystallization method.
14 They also mentioned a new form of ROY.

15 Q. To date, how many forms of ROY have been discovered?

16 A. I believe it's 14 now.

17 Q. And how many of those forms are unsolvated?

18 A. All 14.

19 Q. Okay. And when was the crystalline form of ROY first
20 discovered?

21 A. I think it was around the year 2000.

22 Q. And so is it fair to say that 20 years later, you and
23 other scientists continue to discover new crystalline forms
24 of the compound ROY?

25 A. Yes, that's correct.

Steed - direct

1 Q. Can you predict in advance whether you are going to
2 discover a new polymorphic compound?

3 A. No, not at all. We are were interested in developing
4 new crystallization methods. We tried it on ROY because
5 it's a new and colorful compound. I was surprised we got a
6 new ROY.

7 Q. Have plaintiffs also comment on the predictability of
8 obtaining new crystalline forms?

9 A. Yes.

10 Q. If we could pull up JTX-53. And if we could scroll in
11 there. What is this document?

12 A. So this is the file wrapper of a number '753. I
13 believe it's in the same patent family as the '548 patent.

14 Q. Okay. And if we could turn to page 9 of this document
15 and pull out the paragraph the sentence that's highlighted
16 in the middle there.

17 The author or the patentee is saying, indeed,
18 there is no reliable way of predicting the synthesis of a
19 particular polymorph, or the influence of a particular
20 polymorph on the behavior of a chemical compound, since each
21 polymorph imparts unique properties to the parent compound.

22 Do you agree with this statement?

23 A. Yes, I do. I'm trying to -- there's no way that you
24 can know in advance what the conditions are, what will give
25 rise to a particular polymorph or what properties it's going

Steed - direct

1 to have out doing the crystallization of analyzing the
2 product.

3 Q. All right. So I want to take the discussion that we
4 just had about the specification of the '548 patent and
5 after discovered forms and frame it in the context of that
6 slightly complicated genus analysis that we looked at. If
7 we could pull back up demonstrative 22 and highlight that
8 bottom bullet there.

9 And I want to start with the first prong and
10 discuss whether there are a sufficient number of
11 representative species in the specification for them to
12 claim a genus.

13 Now, again, we discussed earlier how many forms
14 disclosed in the '548 patent specification come within the
15 scope of claim 18.

16 A. There are two forms, A and C.

17 Q. And for claim 19, how many forms disclosed fall within
18 the scope of claim 19?

19 A. Just a single form, A.

20 Q. So in your opinion, are the two species disclosed in
21 the '548 patent sufficient to represent all crystalline
22 forms of ibrutinib that have the properties described by
23 claim 18?

24 A. No. A very small number indeed and it wouldn't be
25 clear to a person what, what this genus would have in common

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1 just by looking at form A and seeing it, two different
2 forms, two different properties in their own right, and it's
3 not clear how you would go on from those two to create the
4 rest of the genus.

5 Q. Okay. And what about for claim 19? Is the single
6 species disclosed in the '548 patent sufficient to tell a
7 POSA that the inventor had invented the entire category of
8 crystalline form that had the properties of claim 19?

9 A. No. A single species, of course, you have no way
10 of knowing what properties the species first have in
11 common or how to get to them because you've only got one
12 to look at.

13 Q. Okay. And now I want to focus on the second prong,
14 which is the structural features common to members of the
15 genus, which is also complicated, but let's see if we can
16 simplify it a little bit.

17 Now, and I want to start with, does it make
18 sense to say that there are structural features of claims 18
19 and 19 that a crystalline form could have in common so that
20 you could visualize the entire genus?

21 A. This doesn't make sense to me in the context of
22 crystal forms. As I said before, in terms of molecules with
23 a particular functional chemical group, you might recognize
24 particular structural features of molecules that might give
25 them properties in common. Certain kind of chemical

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1 reactivity, for example. The polymorphs, each one is
2 unique. Each one forms all by itself based upon the
3 condition in which it finds itself and each one has its own
4 unique structure.

5 So I suppose they may have things in common
6 in the sense that they represent a molecule other than the
7 fact that there's no linking polymorph. Each one is
8 individual.

9 Q. Okay. So now let's go through the structural features
10 plaintiffs claim this genus has in common. And can we bring
11 up slide 6-30.

12 Now, are these the structural features
13 plaintiffs claim the genus or genera of claims 18 and 19
14 have in common?

15 A. Yes. This is what they were able to identify as
16 what's in common within this genus.

17 Q. Okay. Let's go through those one by one. If you can
18 go to the next slide, 31.

19 So do you agree that being a crystalline form of
20 ibrutinib is a feature that is unique to the genera of
21 claims 18 and 19?

22 A. No, not at all. Obviously, by definition, any
23 crystalline form of ibrutinib contains the compound
24 ibrutinib by definition. So, of course, there are
25 crystalline forms of ibrutinib that don't fall within the

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1 scope of claims 18 and 19, so having ibrutinib in them can't
2 be an uniting feature of the genus because there are
3 crystalline forms of ibrutinib that aren't part of the
4 genus.

5 Q. If we can go to the next slide. What are you showing
6 by filling in these two columns, one with A and C and one
7 with A, B, C, D, E and F?

8 A. In this I'm pointing out there are other forms which
9 are crystalline forms of ibrutinib that don't fall within
10 this claimed genus and so therefore having ibrutinib can't
11 be part of the genus because forms B, D, E and F are also
12 crystalline forms of ibrutinib but don't fall within the
13 scope of the claims and aren't part of the genus.

14 Q. Okay. Let's pull up the next slide, which shows
15 plaintiffs' second argument. So next they argue that the
16 2-Theta peaks, 18.9 and 16.1 are a structural feature that
17 unites the genus.

18 Do you agree with that?

19 A. No. There's no structural feature I can recognize
20 that gives rise to 18.9 or 16.1. Whether or not there's a
21 peak in the position is a complex outcome of the way in
22 which the molecules impacts the crystal as a whole, and
23 there's no way to engineer or predict that and even if you
24 had in your hands something that already has a peak in that
25 position.

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1 And, moreover, there are, again, crystalline
2 forms disclosed in the '548 patent that don't fall within
3 the scope of this genus. They don't fall in the scope of
4 claims 18 or 19 but do have two peak to peak at 18.9 and
5 16.1. They're having 2-Theta peaks, those two positions
6 can't be the feature.

7 Q. Okay.

8 A. They don't fall into the claims.

9 Q. If we could pull up the next slide. Is that what you
10 are showing here?

11 A. Yes. So claim 18 was noted to form A and C. Claim
12 19. That's the species falling within the genus
13 interpretation. But, in fact, forms A, C, D and F all have
14 peaks at 18.9 and 16.1. So D and F have the peaks, but
15 they're not part of the genus. That again can't be a
16 feature of the genus.

17 Q. Okay. So let's go to the third argument, the argument
18 that both forms A and I are monoclinic. Do you agree
19 that -- let me start. Do you agree that both form A and I
20 are monoclinic?

21 A. No. In fact, we don't know what crystal class is form
22 I. It hasn't been determined yet. Form A.

23 Q. And why do we not know whether form I is monoclinic or
24 not?

25 A. Well, there's no known crystal structures. We don't

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1 know what its -- both Dr. Myerson and I are taking the X-ray
2 pattern of form I tried to do a mathematical process called
3 indexing and what that does, it derives from the X-ray
4 pattern what the unit cell, the basic building block.
5 Monoclinic is one of just seven categories. And it just
6 means it happens to have one angle of incline.

7 So if we were able to index the pattern
8 successfully, we would have found out if it was monoclinic
9 or not, but neither Dr. Myerson nor I were able to do that.
10 The data was not good enough for indexing.

11 And so we simply didn't, didn't get to a correct
12 solution. We both produced a number of different possible
13 solutions, none of which were very reliable. Some were
14 okay. Some we were trying to make. We don't know if any of
15 those --

16 Q. So to be clear, the data that Dr. Myerson generated
17 and the one you generated in response to that, is that data
18 scientifically reliable in your opinion?

19 A. No, not at all. The computer really wasn't able to
20 find a suitable fit to that pattern, so we don't know
21 whether one of the 20 odd solutions the computer tried to
22 come up with is reliable or it's not reliable.

23 Q. All right. Now, we discussed at form C in claim 18.
24 Is form C monoclinic?

25 A. No, it isn't. It's triclinic.

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1 Q. Okay. How do we know that?

2 A. It's a paper published in 2018 which definitively
3 characterized Form C. Having a full X-ray structure
4 analysis and derived the units and showed that it's
5 triclinic.

6 Q. Okay. If we could pull up DTX-1304. And what is this
7 article, Dr. Steed?

8 A. Yes. This is a paper published in 2018 that I was
9 talking about which did a full crystallographic study on A,
10 B and C.

11 Q. If we could turn to page 1318 of this document, across
12 the table. I see in the third column it says ibrutinib
13 polymorph C?

14 A. Yes.

15 Q. If we go down to the space group, I see it says for
16 form A, it's monoclinic and for form C, it's triclinic; is
17 that correct?

18 A. Yes. It's the crystal system. As I said, it's
19 just --

20 Q. Sorry.

21 A. Monoclinic and triclinic are the common ones and in
22 this particular one, polymorph C was shown to go triclinic.

23 Q. Okay. So we can take that down.

24 If we could pull back up the next slide and go
25 to DDX-6.36. What are you showing here based on what we

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1 just discussed?

2 A. Being monoclinic, like a million other crystals known
3 to science, can't be the defined feature of this genus
4 because form A and C are supposed to be part of the genus,
5 the genus that forms claim 18.

6 Forms C and D are monoclinic, so that can't be a
7 defining feature. And then in terms of other forms in the
8 '548 patent, we just don't know. We don't know the crystal
9 system of some of the other forms. We don't know.

10 Q. Okay. Now, let's go to the second-to-last argument
11 that plaintiffs make and if we go to the next slide.

12 So now they argue that both forms A and I are
13 relatively thermodynamically stable and somehow that is a
14 uniting feature for claim 19 in particular. Do you agree
15 with that argument?

16 A. No, I don't.

17 Q. Why not?

18 A. Well, any given set of conditions, temperature,
19 pressure, one particular polymorph for the most stable and
20 it's always form A and everything else is less stable than
21 form A. In terms of what's meant by relatively stable, I
22 would argue that all of form A, B, C, D, E and F are
23 relatively stable in the sense you can isolate them, you can
24 study them at least long enough to study their X-ray
25 diffraction pattern. As compared to an unstable form,

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1 something that transforms into something else or decomposes
2 before you can study it. All six are relatively stable.
3 Not as stable as A. They're all stable enough to study, so
4 I would say they're thermodynamically stable.

5 THE COURT: Can you stop for one second? You
6 mean form A for ibrutinib? Is that what you are talking
7 about?

8 THE WITNESS: Yes.

9 THE COURT: I just want to make sure. Form A,
10 that's just a name they gave it in terms of ibrutinib.
11 Right? They could have called it form 45. Right? That is
12 just an -- there's no naming convention to that. Is that
13 correct?

14 THE WITNESS: That's absolutely right, Your
15 Honor.

16 THE COURT: Sorry. I wanted to make sure I
17 wasn't missing something. All right. Thanks.

18 BY MS. CLAYTON

19 Q. So in your understanding, which form as between form A
20 and I of ibrutinib is more stable?

21 A. Form A.

22 Q. Okay.

23 THE COURT: Wait, wait. That's where your
24 British accent may have affected us. So it's form A as in
25 apple. Is that right?

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1 THE WITNESS: Yes. "A" as in apple. I
2 apologize.

3 THE COURT: Okay.

4 BY MS. CLAYTON

5 Q. If we could pull up the next slide. So why have you
6 filled in this row in this manner here?

7 A. Yes. Well, as I explain, I would describe all the
8 forms of the '548 patent as being relatively stable because
9 they're stable enough to study. And so being relatively
10 thermodynamic stable can't be a defining feature of this
11 genus because there are forms that are not part of the genus
12 that do have that characteristic.

13 Q. Okay. And if we can go to the last item on the next
14 slide. Next, they argued both A and I are monotropically
15 related. Let's start with, what does monotropically related
16 mean?

17 A. Yes. Complex terms. Actually, it refers to a fairly
18 simple phenomenon. So if two polymorphs are monotropically
19 related, that means one of those two is the most stable
20 throughout the whole temperature range up until the melting
21 point. So in this case, it's true, forms A and I are
22 monotropically related because form A is always more stable
23 than I irrespective of the temperature.

24 There are other examples in other compounds
25 where the temperature, but you have a former high

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1 temperature different than the one that's stable.

2 THE COURT: I'm sorry. I need to put you on
3 hold. We've got something going on here in the building.
4 I'm sorry to interrupt. It's a bad time. Everybody is
5 going to have to wait for a second.

6 (Pause.)

7 THE COURT: Okay. Sorry about that. And we're
8 trying to figure out what's going on, but we can pick up.
9 Apologies.

10 So we left off where there are other examples
11 and other compounds where the temperature, but you have the
12 former high temperature different from one that's stable. I
13 guess I will leave you, Ms. Clayton, to figure out how to
14 pick up.

15 MS. CLAYTON: Sure. Yes.

16 BY MS. CLAYTON

17 Q. So, Dr. Steed, I think you were just describing how,
18 what the difference is between monotropically related and
19 enantiotropically related. I can't even get that word out.

20 Can you describe for the Court the difference
21 between those two?

22 A. Yes. So there's just the two possibilities. You can
23 either be monotropically related or enantiotropically
24 related. And enantiotropically just means that the
25 stability swaps over as a function of temperature, so A is

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1 more stable than I at low temperature and you warm it up and
2 if they were are enantiotropically related, then A is
3 stable.

4 Forms A and I are indeed monotropically related.
5 Form A is the most stable up to the melting point. But so
6 are the other forms. Form A is the most stable out of all
7 the forms described in the '548 patent as well.

8 So, again, being monotropically related can't be
9 feature. There are other forms. Monotropically related
10 that don't fall within.

11 Q. If you pull up the next slide, is that what you are
12 showing here?

13 A. Yes. It is my understanding that form A is the most
14 stable form.

15 Q. Okay. So in sum, after looking at all of plaintiffs'
16 arguments, what is your opinion as to whether any of these
17 structural features unite the genera that are set forth in
18 forms 18 and 19?

19 A. They don't. These are all just general descriptions
20 of many different crystals. They don't seem to define any
21 kind of genus because there are forms that have the feature,
22 have each one of those features that don't inform claims 18
23 and 19. All of these features can't be defining features of
24 the genus that's fall under claim 18 and 19 in this kind of
25 genus argument. It doesn't make any sense.

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1 THE COURT: All right. Hold up one second. So,
2 Ms. Clayton, were you using the word genera, I think.

3 MS. CLAYTON: I was.

4 THE COURT: Okay. Now, genera is plural of
5 genus. Right?

6 MS. CLAYTON: Correct.

7 THE COURT: Okay. All right.

8 BY MS. CLAYTON

9 Q. So in sum, based on all the evidence we just looked
10 at, what is your opinion as to whether as of June 4th, 2012,
11 any of the inventors were in possession of crystalline forms
12 besides A through F?

13 A. They were not in possession of anything other than
14 claims A, B, C, D, E and F.

15 Q. And so in your opinion, does the specification of the
16 '548 patent sufficiently describe any crystalline forms of
17 ibrutinib other than A through F?

18 A. No, it doesn't. It doesn't describe anything other
19 than forms A through F.

20 Q. And so what is your opinion as to whether or not there
21 is sufficient written description support for claims 18 and
22 19 of the '548 patent?

23 A. Insofar as the claim language taken to mean any form
24 with characteristics, any form of ibrutinib with peak
25 positions being unsolvated and the patent, written

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1 description other than form A through F and therefore is
2 invalid for written description.

3 Q. Okay. Now, let's turn to your enablement analysis.
4 I'm hoping we can get through that quickly because we set
5 the foundation with a lot of things you already discussed.

6 And so let's start by reviewing what you
7 understand to be the correct standard to apply. Can you
8 pull up slide 642, please, PDX-6-42.

9 So, again, I know you're not a lawyer, but can
10 you describe for us what you understand you are supposed to
11 analyze for enablement?

12 A. Yes. So my understanding is it's basically the patent
13 has to teach you how to use the invention. So everything
14 that falls under the claims of the patents and the patents
15 actually teach you how to make and use that. In other
16 words, the language says make and use the full scope of the
17 claim. So if the claim claims something, the patent has to
18 teach you how to get to it and make it.

19 Q. And on the second bullet point, do you understand that
20 there are certain factors called the Wands factors you're
21 supposed to apply?

22 A. Yes, that's right. The person of skill being taught
23 by the patent how to make and use the claim should not have
24 to undergo undue experimentation. They shouldn't have to do
25 undue experimentation in order to make and use the full

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1 scope of the patent's claims and the Wands factors is my
2 understanding of the law help us analyze whether the amount
3 of that expectation -- the amount of experimentation that
4 would be required to make and use the full scope of the
5 claim would be undoable.

6 Q. Okay. So let's go through each of those and if we
7 could go to the next slide. And I want to start with the
8 rest of the claims and we talked about this a lot, so I
9 don't want to belabor it, but how would you describe the
10 breadth of claims 18 and 19 of the '548 patent?

11 A. Incredibly broad, potentially unlimited. You wouldn't
12 know if you found all of them that fall under that claim.

13 Q. Okay. And let's go to the next slide. So given the
14 breadth of these claims, how would you describe the nature
15 of the invention here?

16 A. So in this claim, I used the nature of the invention.
17 It's every single form of ibrutinib whether known or not as
18 we sit here today that has peaks in those one or two places
19 and is unsolvated.

20 Q. And so how does that mean you would describe the
21 complexity of the nature of the invention claimed?

22 A. Well, that then becomes very complex. So, one, a
23 person of skill knows how to do a crystallization. They
24 wouldn't know which crystallizations to do in order to get
25 every single form, including ones that are not in science

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1 that might fall under this claim language. That would make
2 it a very complex inquiry indeed, because we don't know when
3 to stop.

4 Q. Okay. And if we could turn to the next slide. What
5 about the state of the art? Was there anything in the art
6 related to either ibrutinib or crystallization generally
7 that helped with the complexity and breadth of the invention
8 here?

9 A. Well, the patent itself teaches how to make six forms
10 of ibrutinib. A person could do that. Beyond that, there's
11 nothing else in the patent. The skilled artisan would know
12 how to do crystallizations. They would know the methods
13 I've described, so they could go crystallize ibrutinib in a
14 different way. Just as long as they avoided the teachings
15 of the '548 patent, they could do something different and
16 might get lucky and get a new form. They also might try
17 to not get a new form of '548. There are already six of
18 them.

19 The point is they wouldn't know which
20 crystallization sayings to do, including crystallization
21 methods not yet invented, which might result in forms that
22 would be covered by the claims. So, for example, I wouldn't
23 know from the prior art how to do a droplet crystallization,
24 because that hasn't been invented yet.

25 Q. Okay. And what about the predictability in the art?

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1 How would you characterize the level of predictability in
2 the art both in making new crystalline forms and knowing
3 what properties those forms are going to have?

4 A. This is an empirical way, the way people can't predict
5 in advance what's going to happen. They just try a
6 crystallization method or set of crystallization conditions
7 and then they see what happens.

8 So there really isn't any predictability other
9 than the predictability that if I bring about a high
10 solution, I might get crystal structures.

11 It is possible to try to calculate crystal
12 structures. They typically give rise to hundreds, if not
13 thousands of possible crystal structures. They give no
14 guidance how to actually make them. The person is left just
15 trying to set the conditions, and in this particular case,
16 it would require the full scope of the claim. That person
17 would be endlessly trying different crystallization
18 techniques and different crystallization variables, never
19 being really sure whether they explored the full scope of
20 the claim.

21 Q. Okay. And, in fact, have plaintiffs characterized
22 crystalline forms of ibrutinib as unpredictable?

23 A. Yes, I believe we could.

24 Q. If we could pull up PTX-2430.

25 Dr. Steed, what do you understand this document

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1 to be?

2 A. So this is a set of plaintiffs' responses to
3 defendants' interrogatories.

4 Q. Okay. And if we could go to the bottom of page 44
5 to the top of page 45. If we could call out Section C
6 there.

7 All right. So you see there the first line says
8 crystal structures and polymorphism are highly
9 unpredictable. A POSA cannot predict whether a particular
10 crystalline form or polymorph can be made or what structure
11 or properties that a crystalline form or polymorph many
12 have. That was true as of June 4th, 2012, and remains true
13 today.

14 Do you agree with that statement as plaintiffs
15 have set it forth there?

16 A. Yes, that's right. You don't know whether you could
17 make it in crystalline form because you don't know what
18 conditions it would be formed under, so they're just left
19 empirically trying potentially endlessly, maybe trying to
20 invent new crystallization methods because you don't know in
21 advance whether you will make it.

22 Q. Now, the level of skill in this art is high. Does
23 that compensate for the fact that this is an unpredictable
24 art?

25 A. No, not really. A person of skill, highly educated,

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1 as I would describe. They would know how to do
2 crystallization. They would know how to do polymorph
3 screening as it's done in industry, which has the goal of
4 identifying the most stable form and the more accessible
5 form, but that's very, very different than trying to
6 identify every single possible form with a particular set of
7 recited and unpredictable characteristics. So a person
8 knows how to crystallize, but they don't know how to
9 crystallize every possible form.

10 Q. All right. If we could go to the next slide. One
11 more after that, 48. We've already discussed it
12 extensively, too. I just want to touch on it for a moment.

13 Is there a specific direction or guidance given
14 in the specification or examples given in the specification
15 that would teach a person how to make all crystalline forms
16 of ibrutinib that are recited in claims 18 and 19?

17 A. No, there is detailed guidance on how to make the six
18 forms that are disclosed in the patent and that's where the
19 patent stops. There's no other guidance on this patent.

20 Q. Okay. And I want to conclude with the last one. Go
21 to the next slide. Quantity of experimentation.

22 Again, you've touched on this a little bit in of
23 some your last answers. In your opinion, given the scope of
24 the claims here, how much experimentation would be necessary
25 in order for a highly skilled person to make and use the

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1 full scope of the claims that are at issue here?

2 A. Yes. The full scope is key here. In the context of
3 experimentation, it's potentially unlimited. You could go
4 on until you ran out of patience, money, or years of life
5 and never be sure you had made and used the full scope of
6 the invention.

7 Q. In your background on the technology tutorial, you
8 discussed a variety of variables that can influence the
9 crystalline form of ibrutinib or any crystalline form that
10 you get.

11 Do you recall that testimony?

12 A. I do.

13 Q. And if we could bring up slide DDX-6-58 again.

14 So tell us, how do these variables influence the
15 amount of experimentation that would be required to practice
16 the full scope of the claim?

17 A. Yes. Well, there's a potential, very, very large
18 experimental space using -- it varies from parameter to
19 parameter that could result in a potential new form of
20 ibrutinib, particularly crystallization method.

21 Some crystallization methods are being invented
22 at the time. Without knowing at the time of the filing of
23 the patent, it may not have been invented yet. There could
24 always be a new crystallization method that gives rise to a
25 polymorph of the scope of the claims that a person would

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1 have to invent effectively and even coming to more ordinary
2 things like changing the solvents.

3 Again, they could keep changing solvent and
4 solvent mixtures with different temperatures, cooling rates,
5 concentrations, pH and so on, essentially endlessly. They
6 might just keep getting the same form. They will never know
7 whether they just assumed they have not explored the space
8 enough or whether there were no more forms to be had, and
9 not knowing whether you, whether you've finished.

10 Q. And have plaintiffs also previously described the
11 amount of experimentation that is required to make
12 crystalline forms of ibrutinib?

13 A. Yes, they have.

14 Q. If we could go back to DTX-2430 again. Turn to page
15 47 of this document.

16 Do you see where they say, a POSITA an
17 attempting to make a crystalline form or forms of ibrutinib
18 would have to have had performed extensive trial-and-error
19 experimentation, using an enormous number of variables and
20 conditions, and would not have been able to predict the
21 results of such experiments.

22 Is this what you were just describing here in
23 terms of the level of experimentation required in obtaining
24 crystalline form?

25 A. Yes and no. This is describing, attempting to make a

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1 crystalline form. It may not be nothing to make a
2 crystalline form. You may luck out and get one. But
3 the crystalline part requires the full scope of the
4 invention.

5 So a person trying to make all possible
6 crystalline forms falling under these claims would have to
7 perform limitless trial and error experimentation as the way
8 things are described.

9 Q. In sum, based on all the factors we just looked at,
10 what is your opinion whether it would require undue
11 experimentation to practice the full scope of claims 18 and
12 19 of the '548 patent?

13 A. It would indeed require undue experimentation. The
14 full scope is potentially unlimited.

15 MS. CLAYTON: Thank you. We'll turn the witness
16 over for cross-examination.

17 THE COURT: Thank you very much.

18 Doctor, I don't know. Did you want to take a
19 break before we begin cross?

20 THE WITNESS: I'm happy to continue, Your Honor,
21 if you are.

22 THE COURT: Mr. Sipes, how long do you think
23 you'll be? I mean, if we take a break now, do you want to
24 take a break in the middle of your cross? How do you want
25 to do this?

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1 MR. SIPES: Your Honor, I'm happy to proceed
2 however you prefer. The cross won't be too extended. It
3 could be an hour. This is a technical subject matter. I'm
4 happy to take a break whenever Your Honor would want to take
5 a break.

6 THE COURT: All right. If the witness at any
7 point wants to take a bathroom break, that's fine, but,
8 you know -- actually, Doctor, assuming we're going to be
9 like another hour-and-a-half, are you set to go all the
10 way through an hour-and-a-half or would you rather have a
11 break?

12 THE WITNESS: Maybe I will take Your Honor up
13 and I will take a break.

14 THE COURT: I know it's late over there. Is it
15 8:15 or 9:15?

16 THE WITNESS: 8:15.

17 THE COURT: 8:15. So why don't we take a
18 ten-minute break. All right? We'll begin at 3:25. All
19 right. Thank you.

20 MR. SIPES: Thank you, Your Honor.

21 THE WITNESS: Thank you, Your Honor.

22 (Short recess taken.)

23 - - -

24 (Proceedings resumed after the short recess.)

25 THE COURT: Okay. Are we all here?

Steed - cross

1 MR. SIPES: We're here Your Honor.

2 THE COURT: Proceed then, Mr. Sipes.

3 MR. SIPES: All right.

4 CROSS-EXAMINATION

5 BY MR. SIPES:

6 Q. Good evening, I guess, Mr. Steed. My name is
7 Christopher Sipes. I'm here on behalf of plaintiffs. I'm
8 in Washington, D.C., so I appreciate you joining us from
9 England.

10 Let me start with something that I think
11 everyone agrees on. Both you and Dr. Myerson agree that the
12 POSA here is highly skilled; correct?

13 A. Yes.

14 Q. And you agree that the '548 patent discloses all the
15 crystalline forms of ibrutinib that have been made prior to
16 the filing date for the patent; is that correct?

17 A. That's my understanding, yes.

18 Q. So the '548 patent disclosed all the crystalline forms
19 of ibrutinib that were known in the art at the time of the
20 filing of the patent; is that correct?

21 A. That's my understanding.

22 Q. And crystalline forms A through F are each enabled by
23 the disclosure of the '548 patent; correct?

24 A. Yes, that's my understanding. That's right.

25 Q. And there is adequate written description for

Steed - cross

1 crystalline forms A through F in the '548 patent; is that
2 correct?

3 A. Yes.

4 Q. So which is to say that the '548 patent enabled a
5 person of ordinary skill in the art at the time to make an
6 use all of forms A through F; correct?

7 A. Yes, I would agree with that.

8 Q. Now, let's look a little bit at the scope of claims 18
9 and 19. You understand that those are the claims that are
10 at issue in this proceeding, claims 18 and 19 of the '548
11 patent; correct?

12 A. Yes, I do.

13 Q. So let's turn, if we could, Mr. Brooks, to DDX-6-25.
14 DDX-6-25 is actually drawn from an exhibit, Exhibit 4 that
15 you put together in your expert report identifying
16 crystalline forms from after the '548 patent; is that right?

17 A. Yes, that's right.

18 Q. And if you go to DDX-6-25, there's a number of forms
19 and you've sorted the forms that, on the right-hand column,
20 the source. You went into the literature and you surveyed
21 the literature to find additional crystalline forms of
22 ibrutinib; is that correct?

23 A. Yes, that's right.

24 Q. And you've identified a number of forms and then when
25 you get down to claim 18 and 19, there are two forms that

Steed - cross

1 you've identified within claim 18 and that's form I and form
2 S3.

3 Do you see that?

4 A. That's right.

5 Q. And you note that those two forms are unsolvated;
6 correct?

7 A. Yes.

8 Q. And of all the forms that are on this exhibit,
9 DDX-6-25, those are the two forms that are unsolvated, form
10 I and form S3; is that correct?

11 A. Yes.

12 Q. So you're not aware of any crystalline forms of
13 ibrutinib that are not either disclosed in the '548 patent
14 or listed here on this exhibit that we're looking at now;
15 correct? DDX-6-25?

16 A. That's right, yes. This wasn't an exhaustive search,
17 but these are the ones that I'm aware of.

18 Q. So we can say that you and me and everyone else is
19 aware of five unsolvated forms of ibrutinib, forms A, B, C,
20 I and S3; correct?

21 A. Yes, as far as I'm aware.

22 Q. Now, we've talked a lot and you even in your testimony
23 earlier today have talked about unsolvated forms and you
24 agree that claims 18 and 19 are limited to unsolvated forms
25 of ibrutinib; is that correct?

Steed - cross

1 A. Yes, that's right.

2 Q. But I'm not sure you explained in your tutorial what
3 that means, an unsolvated form versus a solvated form, so
4 let's see if we can get to a little bit of that.

5 In a solvated form, solvent molecules are
6 incorporated into the crystal lattice along with the
7 molecule of interest, if you will; correct?

8 A. Yes, that's the regular repeating part of the crystal.
9 Not just a wet crystal. They're actually a tangible part of
10 the structure.

11 Q. There's an intellectual concept called a unit cell,
12 which is really describing the repeating unit of the
13 crystal. It's made up of the various molecules that are in
14 the crystalline lattice; is that correct?

15 A. I wouldn't quite agree with that. I know what you are
16 getting at. It would be the mathematical concept about the
17 way we describe how they impact. The units are not made up
18 of molecules. Usually drawn as a box around the molecules.
19 I think I see what you mean that.

20 Q. What's defining the unit cell is the structural
21 arrangement of the molecules in crystal. Is that fair?

22 A. No, absolutely not. The structure of the molecules
23 comes from an attempt to see. The unit describes the
24 periodicity with the heat in the crystal.

25 Q. Are you really saying that the unit cell has nothing

Steed - cross

1 to do with the packing of the molecules in the crystal?

2 A. The unit cells are a concept that describe the
3 symmetry, the way in which the molecules pack, but it
4 doesn't describe molecular structure.

5 Q. Okay. That's what I was getting at. You are trying
6 to describe how the molecules and the crystals are packed.

7 A. Yes. It's how we describe the packing arrangement.

8 Q. So in a solvate, in addition, in an ibrutinib --
9 excuse me. In an ibrutinib solvate, you would have in a
10 repeating pattern not just ibrutinib, but one or more
11 additional solvents present; is that correct?

12 A. Yes, that's right.

13 Q. And a solvent could be as simple as water; right?

14 A. Yes. That would make it a hydrate, which is an
15 example of a solvate, yes.

16 Q. It could be other solvents like toluene or acetone or
17 isopropyl alcohol. There's a wide variety possible of
18 solvates?

19 A. Yes, that's true.

20 Q. And so it's not surprising to find more solvates of a
21 molecule than unsolvated forms; is that correct?

22 A. It just depends completely on the molecule. Some
23 molecules don't form solvates at all. Others form a lot of
24 solvates.

25 Q. So let's focus on -- this case is focusing on

Steed - cross

1 unsolvated forms.

2 Now, you pulled up an article and we can take a
3 look at it. This was called ROY. That's the name of the
4 compound, reclaimed its crown.

5 Do you recall that?

6 A. I do.

7 Q. And the reason that ROY is reclaiming its crown is
8 because it is the king of polymorphic forms that are
9 unsolvated; is that correct?

10 A. Not quite sure what you mean by king. The crown has
11 been referred to in the literature is having the most single
12 crystal X-ray structures of any -- of any particular
13 compound. Of course, it's not surprising because ROY has
14 extensively studied, it's an attractive visual and it's a
15 great test.

16 Q. In fact, ROY has 14, 14 unsolvated forms; is that
17 correct?

18 A. Yes.

19 Q. Now, in terms of your, the compounds that you've
20 worked with, you don't recall, when you were at the
21 deposition, you don't recall working on a compound with more
22 than four unsolvated forms; is that correct?

23 A. I didn't initially recall, and then I remembered
24 carbamazepine.

25 Q. And so that gives us a sense of unsolvated forms when

Steed - cross

1 you start to get to, you know, the number of unsolvated
2 forms that you typically find in molecules. ROY is unusual,
3 you would agree with that; is that correct?

4 A. ROY is extensively studied, so any new method, they
5 try to try them out. It's a popular example.

6 Q. Well, I'm looking at the list of sources that you have
7 for crystalline forms of ibrutinib on DDX-625. That's
8 looking like it's pretty extensively studied, too, is it
9 not?

10 A. Not so much in the academic literature. It's
11 obviously in the interests for commercial use of the
12 patent.

13 Q. So let's come back to unsolvated forms because that's
14 really what's at issue in this case, correct, is unsolvated
15 forms?

16 A. In terms of claim 19, yes.

17 Q. And I think if we look -- keep looking at DDX-625.
18 You identify two additional unsolvated forms that are within
19 claim 18, form I and form S3. We went through that; is that
20 correct?

21 A. That's what we've learned so far.

22 Q. And, of course, we know that two other unsolvated
23 forms, forms A and C, that are described and enable by the
24 '548 patent, also fall within claim 18; is that correct?

25 A. That's my understanding, yes.

Steed - cross

1 Q. So what we know and what we can say is that there are
2 four known forms of ibrutinib that fall within claim 18; is
3 that correct?

4 A. That's what we know about so far, yes.

5 Q. Now let's look at your chart for claim 19. For claim
6 19, you identified one additional form, form I. Correct?

7 A. Yes.

8 Q. And, of course, we know that form A, which is
9 described in the '548 patent, also falls within claim 19; is
10 that correct?

11 A. Yes.

12 Q. So sitting here today, we know that there are two
13 unsolvated forms of ibrutinib that fall within claim 19?

14 A. There are two that have been discovered so far that
15 are important.

16 Q. So we can refer -- we can refer to claim 19 as a
17 genus, but it is a genus that at least to date is a genus of
18 two; is that correct?

19 A. I wouldn't refer to a crystalline form in the context.

20 Q. Okay. There are two individuals within claim 19; is
21 that correct?

22 A. Yes, and the way that these patents are, the claim
23 construction.

24 Q. Now, I think we have talked about form I. You
25 talked about it with your counsel, that it was relatively

Steed - cross

1 stable.

2 Do you recall that?

3 A. Yes.

4 Q. And, in fact, in your own rebuttal report, you have a
5 whole section about the fact that form I has polymorphic
6 stability; is that correct?

7 A. Yes. The phrase relatively stable obviously is
8 subjective. As I explained, I find them to be stable --

9 THE COURT: Wait, wait. Sorry. He defined
10 relatively stable as, and then there was movement of the
11 microphone and we missed it.

12 So relatively stable and what?

13 THE WITNESS: Stable enough to study.

14 THE COURT: Okay. Thank you.

15 THE WITNESS: I wouldn't characterize the form
16 as unstable.

17 MR. SIPES: Actually --

18 THE COURT: No. We missed your last sentence.
19 "I wouldn't characterize the form as unstable," and then
20 whatever you said.

21 THE WITNESS: If it's stable enough to study,
22 record a powder diffraction pattern?

23 THE COURT: Record a powder diffraction
24 something what?

25 THE WITNESS: Pattern.

Steed - cross

1 THE COURT: Pattern. All right. Thank you.

2 BY MR. SIPES:

3 Q. Now, in your rebuttal report, you actually went much
4 further. You pointed out that form I is sufficiently
5 stable, that it does not change the polymorphic form during
6 manufacturing of the product, nor does it change its
7 polymorphic form during storage; is that correct?

8 A. That's my understanding. It does seem to be stable
9 under those conditions.

10 Q. So rather than relatively stable, would you prefer the
11 term quite stable?

12 A. I think these are all subjective terms. My
13 understanding is it's less stable than form A, but it is
14 relatively stable, quite stable.

15 Q. There are polymorph forms that turn out not to be
16 useful in pharmaceutical manufacturing because they do
17 change forms either in manufacture or storage; is that
18 correct?

19 A. Yes, that's right. Stability is a bit of a gray scale
20 from that point of view.

21 Q. But one thing we know about both form A and form I is
22 they have an attribute of stability which enables them to be
23 manufactured into drug products and then stored long term
24 without changing polymorphic form; is that correct?

25 A. I suppose if appropriately handled, you would have to

Steed - cross

1 do that.

2 THE COURT: Hold up. Sorry. Mr. Sipes, I think
3 what's going on, too, I think when you move your notebook,
4 it takes over the microphone. That's part of it.

5 MR. SIPES: Right.

6 THE COURT: So sorry to interrupt. I don't like
7 to interrupt cross-examination, but we've got to get this on
8 the record.

9 So, Doctor, if you could maybe get closer. It
10 was better before. It's wherever you're positioned on the
11 mike. You seemed closer actually than you were in your
12 direct. Where is your microphone?

13 THE WITNESS: It's just right above my -- I have
14 one pointing. I have one above my screen.

15 THE COURT: Now we can hear you, so let's repeat
16 what's the last question. And maybe it's not Mr. Sipes,
17 but somebody is moving and then that interrupts the
18 microphone.

19 MR. SIPES: I will take the blame for it, Your
20 Honor. I don't know that it's me, but I am of a bit of a
21 fiddler. It's probably me.

22 THE COURT: All right. So let me back up and
23 see where we lost it.

24 So your voice does tend to go down when you
25 answer. All right.

Steed - cross

1 So the question that was put to the witness was:

2 "But one thing we know about, both form A and
3 form I, is they have an attribute of stability which enables
4 them to be manufactured into drug products and then stored
5 long term without changing polymorphic form. Is that
6 correct?

7 "Answer: I suppose if appropriately handled,
8 you would have to," and then we lost you. All right.

9 THE WITNESS: Have to carry on testing on any
10 given form to see what conditions it was to be stored under
11 in order to see whether it would transform into another form
12 under those conditions and typically, that's what's done
13 within pharmaceutical product development.

14 BY MR. SIPES:

15 Q. And you may recall, you cite in your rebuttal report
16 the study that Sandoz did at different temperatures and
17 humidity conditions for at least three months and for
18 storage for at least one year showing that under those
19 conditions, it remained form I. It was stable under those
20 conditions and that duration; correct?

21 A. Yes. Absolutely right. Any pharmaceutical company
22 wanting to manufacture a drug product would attempt to
23 ensure that it's stable in storage. That's an FDA
24 requirement.

25 Q. In fact, the reason that Sandoz studied it under

Steed - cross

1 different temperatures and humidity conditions is because
2 FDA doesn't assume that everything is perfectly and properly
3 handled. People store their drugs in their medicine cabinet
4 in their bathroom, possibly the worse place.

5 So, in fact, what we've shown is that both form
6 I and form A are pretty rugged and that they are
7 appropriately stable for use in the drug product that's
8 going to be in people's houses; correct?

9 A. I'm not sure I quite characterize it like that.
10 Sandoz has developed a robust product which is stable
11 under the conditions of recommended storage. We do know
12 that form A is more stable than form I. Fortunately,
13 there's a sufficient kinetic barrier. Form I doesn't
14 convert to form A under the recommended handling and storage
15 conditions.

16 Q. It's not just that form I doesn't convert to form A,
17 it doesn't convert to a different crystalline form. It
18 remains form I; is that correct?

19 A. Yes, that's correct. It remains as needed.

20 Q. And I think you said Sandoz developed. Sandoz did not
21 develop form I; is that correct?

22 A. No. I don't think they're the patentee. I think they
23 license it.

24 Q. They purchase form I from a manufacturer abroad; is
25 that correct?

Steed - cross

1 A. I'm not super familiar with the commercial details,
2 but, yes, they do get it from another manufacturer.

3 Q. And so the X-ray powder -- well, let's pull up
4 DDX-610 -- I'm sorry. 611. So you're trying to show how
5 the X-ray powder diffraction pattern is coming out of sort
6 of this repeating arrangement of molecules and crystal; is
7 that correct?

8 A. Yes, the X-ray powder diffraction, it's a
9 characteristic thing of the crystal structure.

10 Q. So you can call it a fingerprint, but there's a big
11 difference between an X-ray powder diffraction pattern and a
12 fingerprint, and that is the X-ray powder diffraction
13 provides information relating to the structure of the
14 crystalline form; is that correct?

15 A. Yes. The whole pattern is determined by the crystal
16 pattern arrangement of the crystal structure.

17 Q. And your fingerprints obviously don't say anything
18 about how tall you are or how wide you are or what you
19 weigh; correct?

20 A. I guess not. It's used for analogy, but it does fall
21 down at some point.

22 Q. And the X-ray powder diffraction pattern is directly
23 related to the crystal structure in the substance; correct?

24 A. Yes. It comes in a what's called transposition from
25 the structure. That doesn't mean to say you can recognize

Steed - cross

1 the structure by looking at the X-ray pattern. You can't
2 really work backwards.

3 Q. And the position of the peak in an XRPD pattern are
4 determined by the unit cells in the crystalline form; is
5 that correct?

6 A. Yes, that's right.

7 Q. And so the position of the peak in an XRPD pattern
8 stems directly from the size and shape of the unit cell and
9 it is the unit cell and only the unit cell that governs the
10 position of the peak; is that correct?

11 A. Yes, that's correct. The positions come directly from
12 the mathematical cell peak. That's how we mathematically
13 treat peaks.

14 Q. And when we refer to position of peak, that is
15 sometimes referred to as the 2-Theta values; is that
16 correct?

17 A. Correct.

18 Q. And I think as we discussed earlier, the unit cells
19 of crystalline form is a representative description of how
20 the molecules are packed to form the crystal; is that
21 correct?

22 A. Yes. Symmetry relationships between the crystal
23 packing arrangement.

24 Q. I don't know if you were trying to show the lattice in
25 your diagram, but the distance between the lattice plane as

Steed - cross

1 defined by the unit cells of the crystalline form is a
2 called the D spacing; correct?

3 A. Yes, that's right. The D spacing is the distance
4 between the planes. It's a mathematical relationship.

5 Q. And we're starting to get into some of the dimensions
6 of the unit cell when you start talking about the D spacing
7 for the lattice plane; is that correct?

8 A. Yes, I suppose so.

9 Q. And the 2-Theta peaks of the XRPD pattern is
10 equivalent to the D spacings; is that correct?

11 A. Yes. They are mathematically related.

12 Q. So each 2-Theta peak position specifies a particular
13 d-spacing of the crystalline form; is that correct?

14 A. Well, the unit cell tells you where the, where the,
15 where the particular reflections from each of the planes in
16 the crystal will come but it doesn't tell you about whether
17 there will be any intensity there, by the unit distribution.
18 The unit cell would tell you to go to look at a 2-Theta
19 position for that particular plane. If they weren't on that
20 claim, you wouldn't get a peak.

21 Q. But you can when you get the peak go back and
22 calculate sort of the D spacing; is that correct?

23 A. Yes. Each peak is mathematically related to D
24 spacing. They are interchangeable.

25 Q. So a 2-Theta peak position of 18.9 degrees corresponds

Steed - cross

1 to a 4.69-angstrom D spacing?

2 A. I can't do the math as I sit here, but that sounds
3 about right.

4 Q. And similarly, a 2-Theta peak position at 16.1 degrees
5 corresponds to a 5.5-angstrom d-spacing?

6 A. Yes. Those are mathematically equivalent. You're
7 saying the same thing.

8 Q. So claim 19 of the '548 pattern specifies unsolvated
9 crystallinity with interplanar spacing separated by 4.69 and
10 5.5 angstroms; correct?

11 A. Yes. That would be mathematically equivalent.

12 Q. And, but by convention, a lot of people in the art
13 often identify crystalline forms by their XRPD pattern
14 rather than doing the mathematical calculation to try to
15 define the unit cell?

16 A. Yes. There would be no reason in doing that to just
17 look at a XRPD pattern.

18 Q. The XRPD pattern is a unique signature that is
19 inherent in a crystalline form; is that correct?

20 A. Yes, that's right. The pattern as a whole could stem
21 from that particular pattern arrangement.

22 Q. And the XRPD pattern is used to distinguish one
23 crystalline form from other crystalline forms of a
24 substance; correct?

25 A. Yes, that's right.

Steed - cross

1 Q. And a crystalline form of a substance is typically
2 identified by a list of characteristic peak positions in its
3 XRPD pattern; correct?

4 A. Yes, with the sense that the United States
5 Pharmacopeia recommends the ten strongest peaks. That is a
6 common shortcut. As I have testified, it's the whole patent
7 that is really characteristic. It's often a convenient
8 shorthand to shorten that down to a representative number of
9 peaks as long as you show those peaks, you need to find a
10 particular crystalline for it.

11 Q. When you are dealing with a known substance rather
12 than an unknown substance, you can often use fewer
13 characteristic peaks to identify a particular crystalline
14 form because you're already starting with the information of
15 what the compound is; is that correct?

16 A. Well, if you mean the chemical compound, then, no,
17 that would be dangerous, but if you know the universe of
18 crystal forms and you're trying to distinguish between them,
19 then you might count a small number of characteristic peaks
20 as long as you are sure there's no chance that something
21 untoward is able of happening.

22 Q. Well, for example, the '548 patent identifies
23 crystalline form B using five 2-Theta peak positions;
24 correct?

25 A. I don't recall a patent. If it lists wide

Steed - cross

1 characteristic peaks, then maybe it does.

2 Q. And the '889 patent, what you testified this morning
3 that form I in claim 1 is identified form I using three
4 characteristic peaks; is that correct?

5 A. Well, I think it tried, the claim language is written
6 such as the claim for three peaks.

7 Q. And this is not out of the ordinary in the art that
8 when you are specifying a crystalline form, a known
9 crystalline form of a compound -- when you specify a
10 crystalline form of a known compound with use fewer peaks
11 than the ten that the USP recommended for unknown compounds;
12 correct?

13 A. The USP isn't recommending any molecular compound.
14 It's saying when you are comparing an unknown sample that's
15 standard, then you should at least stand for these peaks.
16 What tends to happen, if you happen to know you've got two
17 different forms and you want to teach somebody how to
18 quickly and easily distinguish between them, then maybe you
19 might say, yes, just look at these particular peaks. But
20 that's a well validated analytical experiment. That's not
21 the same as producing a complete unknown and then saying,
22 this must be the same as this other form.

23 Q. Now, it is possible for some crystalline forms to over
24 time, sometimes rapidly, convert from one form to another;
25 correct?

Steed - cross

1 A. Certainly.

2 THE COURT: All right. Again, just let's slow
3 down a little bit, both of you. Okay. Sorry. It's just so
4 hard to do this remotely. Go ahead.

5 BY MR. SIPES:

6 Q. In fact, one way with conversion sometimes happening,
7 during the crystalline process, a crystalline form may
8 go from one form, metastable form to another form while
9 it's crystallizing. It changes its crystal lattice;
10 correct?

11 A. Well, there are all kinds of different circumstances
12 under which less stable forms can convert to more stable
13 forms. During the crystallization process, I suppose so,
14 yes, in the sense that one form can form and then -- yes.

15 Q. And let's talk a little bit about crystallization
16 methods. If we can turn to DDX-6-50.

17 THE COURT: Hold on a second, please. Okay.

18 Thank you.

19 BY MR. SIPES:

20 Q. In DDX-6-50, you've given a number of examples of
21 crystallization methods. Evaporation, cooling, melting,
22 milling.

23 Do you see that?

24 A. I do.

25 Q. Now, there is a very well-known crystallization method

Steed - cross

1 in the pharmaceutical arts that you don't identify there,
2 correct, known as seeding?

3 A. I didn't list them all. Seeding is certainly used,
4 yes.

5 Q. Seeding, in fact, is a widely known crystallization
6 method; is that correct?

7 A. It's what's called a secondary crystallization method.
8 If you want to generate a known crystal form from, for
9 example, a supersaturated solution, then you can add a seed
10 of that known in order to, in order to help it to form.

11 Q. And, in fact, seeding is not new. It's a very old
12 form of crystallization; is that correct?

13 A. I suppose so, yes.

14 Q. In your testimony, you had mentioned some method being
15 new. Seeding is not. Seeding is very old?

16 A. Yes. That's fine, and there are various kinds of
17 seeding. We've known for awhile the technique of seeding
18 solids.

19 Q. And seeding, what seeding is, if you have a solution
20 of a compound and you add a tiny amount of crystalline
21 material, that can trigger what's called nucleation,
22 starting to form a crystal lattice that will then quickly
23 grow and you'll get crystallization. Is that a fair
24 description of seeding?

25 A. No. It doesn't assist nucleation. The seed acts as a

Steed - cross

1 secondary nucleus. It is the nucleus and that seed grows
2 into a crystal because it's already there as it were.
3 Seeding is 2020 very, very broad word. For example, Jim
4 Weekes' seeding method is brand-new, 20202. A type of
5 seeding that Jim invented.

6 So seeding certainly exists, was known, but
7 there is variations within seeding as well.

8 Q. But the tiny crystal serves as a platform on which the
9 crystal grows or a template, however you want to describe
10 it?

11 A. They bias the growth rate in favor of the pre-existing
12 seed rather than what we call primary nucleation, which
13 would be creating a new nucleus spontaneously.

14 Q. Well, let's come back. It's not always the case, is
15 it, that when you seed with a particular crystalline form,
16 what you get out of the solution is that crystalline form.
17 In fact, sometimes it will then convert to a different
18 crystalline form than the one you've seeded; correct?

19 A. Well, there's all sorts of possibilities depending
20 upon conditions that typically, when one is seeding, you
21 want to get out the seeded form that you put in unless
22 you're doing something fancy, Jim Weekes did.

23 THE COURT: Hold up. Like Jim what?

24 THE WITNESS: Jim Weekes hetero-seeding.

25 THE COURT: Jim Weekes. Hetero-seeding. Thank

Steed - cross

1 you.

2 BY MR. SIPES:

3 Q. Dr. Steed, let's look at a document, I think it's
4 actually in your direct binder. It's one that you cited in
5 your report and that was identified for you during your
6 direct examination. That's JTX-506.

7 THE COURT: Hold on a second. All right. Go
8 ahead.

9 BY MR. SIPES:

10 Q. Do you recognize JTX-506 as an article in the solid
11 state chemistry, I don't want to call it -- the crystalline
12 form literature that you cited and reviewed in forming your
13 opinions in this case?

14 A. Yes, I do. It has been a while, but, yes.

15 Q. And it's about -- it's called disappearing polymorphs
16 revisited, but it's about polymorphism?

17 A. Yes.

18 Q. And if you will turn to JTX-0506-0003, which is to say
19 the third page, and let's blow up the first paragraph and
20 the heading 2.2, seeds and seeding.

21 Do you see there's a section on seeds and
22 seeding; is that correct?

23 A. Yes.

24 Q. And it says, the 1995 review also contains a section
25 headed seeding. Intentional seeding is a well-known

Steed - cross

1 technique for inducing crystallization and is widely used,
2 especially in the pharmaceutical industry.

3 Do you see that?

4 A. Yes, I see that.

5 Q. And that is true, is it not?

6 A. Yes. It's often used in, for example, large
7 production batches to ensure that the same form comes out.

8 Q. And then it even refers to unintentional seeding
9 arises from the presence of small amounts. In indeed, in
10 principle, one particle is sufficient.

11 Do you see that.

12 A. I do see that.

13 Q. And you concede to create crystallization with very
14 trace small amounts of crystals and it will cause
15 crystallization; correct?

16 A. Yes. I'm not sure it's really known exactly what the
17 practical limit is. It seems to be one or two percent from
18 testing that I've seen.

19 Q. This is an article that you cited in your report;
20 is that correct? It's a reliable article; is that correct?

21 A. It's a -- it is a reliable article in the sense that
22 it's an anecdotal kinds of article. They point out here no
23 one really knows how much is required. Tests on seeding
24 generally fall between one and two percent.

25 Q. Then if we turn to the next page, you'll see there's a

Steed - cross

1 reference to a classic text by Wiberg.

2 Do you see that? Pull that up. That's you see
3 that? Classic text by Wiberg?

4 A. I see the words, yes.

5 Q. And then let's see what he's quoting from Wiberg.

6 Wiberg is a well-known text in the art of crystallization;
7 is that correct? In solid chemistry?

8 A. I confess it's not a book that I'm familiar with.

9 Q. Okay. It notes, when a compound is prepared for the
10 first time in a laboratory, it is often observed that it is
11 relatively difficult to effect crystallization. However,
12 once the compound has been obtained in the crystal state, it
13 is usually easy to effect crystallization, and it has been
14 suggested that after initial crystallization, and, crystal
15 nuclei are present in the laboratory and induce
16 crystallization?

17 A. I do see that.

18 Q. There is this idea of seeding and perhaps even
19 unintentional seeding; correct?

20 A. Yes. This is a hypothesis. It has never really been
21 proven. I think what it does, it reflects the
22 unpredictability of crystallization because it relies upon
23 an individual nucleation and sometimes it can, it can behave
24 in ways that are different to the rest of chemistry.

25 So this is a common anecdote that's told.

Steed - cross

1 Nobody knows whether it's true or not, but it's an
2 attractive speculation.

3 Q. It's an attempt to explain a common observation that
4 it seems relatively difficult to make the first crystal, but
5 once the compound has been crystallized, it seems easier to
6 make crystals after that?

7 A. Yes. It's anecdotal. This is one speculation on it.

8 Q. And let me ask you, and I want to be careful here.
9 You will recall there was some discussion about conversion
10 from form C.

11 Do you recall that?

12 A. You'll have to fill me in with the context.

13 Q. Did you discuss the possibility of starting with form
14 C and convert form C in ibrutinib -- we can take this down,
15 and converting to another crystalline form?

16 A. Are you referring to the testimony in the context of
17 the production process for form I and form C was involved in
18 that? Is that what you mean?

19 Q. That would be one discussion, but, generally, yes.
20 Let's start with that. There are times when one crystalline
21 form is converted to another synthetically; correct?

22 A. I think in that particular case, form C is being
23 crystallized as form I.

24 Q. Did counsel ask you whether you were aware, whether
25 the patent, the '548 patent teaches anything about

Steed - cross

1 converting from one form to another?

2 A. I think counsel asked me whether the patent teaches
3 treating form C with methanol water results in form I. I
4 answered that it did not.

5 Q. The '548 patent does teach conversion of form C to
6 other forms, does it not?

7 A. You'll have to refresh my memory.

8 Q. That's quite all right. Why don't we turn to JTX-0001
9 at 00062.

10 MR. SIPES: Mr. Brooks, let's start with the
11 right-hand column and in form D, that's at column 66, lines
12 17 to 25 many.

13 BY MR. SIPES:

14 Q. So there it refers to creating a dry mixture of two of
15 forms A, B or C, then a slurry with an amorphous MIBK and
16 ultimately, what you get is form B?

17 Do you see that?

18 A. Yes.

19 Q. So that's one way in which one can start with one
20 crystalline and crystalline form and form another; is that
21 correct?

22 A. It looks like it doesn't matter what crystalline form
23 is started with here. It can be any form, A, B or C or
24 amorphous. This is C.

25 Q. Okay. Let's look at that. We can turn to column 65,

Steed - cross

1 Mr. Brooks, and let's pull up from line 44 to 58.

2 Here, it refers to compound one, form A, that's
3 form A, ibrutinib; is that correct?

4 A. Yes.

5 Q. Was weighed into a vessel and dissolved in methanol;
6 is that correct?

7 A. Right.

8 Q. Water is later added; is that correct? Two lines
9 down?

10 A. Yes.

11 Q. Then seeds of ibrutinib form C were added. Correct?
12 Ultimately, at the bottom, what comes out is compound one,
13 form B?

14 A. Yes. Material converted to compound one, form D, B
15 conversion.

16 Q. So seeding with form C in methanol water resulted in
17 form B, according to the teachings of the '548 patent; is
18 that correct?

19 A. I don't think I would quite characterize it like that.
20 What it seems to be the case, seeding with form C produces
21 form C, but that converts to form B. It shows the materials
22 are converted to form B.

23 Q. It is -- so it is, in fact, a method that, a route
24 that's described, it's described as form B, Route one at the
25 top; right?

Steed - cross

1 A. Yes.

2 Q. And the route that's described is using a seeding with
3 form C in a methanol water solution of ibrutinib, ends up
4 with form B; is that correct?

5 A. It ultimately does end up with form B. I think of it
6 as a complex, multistage procedure.

7 Q. Now, methanol and ethanol are pretty similar, are they
8 not?

9 A. It depends. They have similar properties.

10 Q. I don't recommend drinking ethanol, but they are both
11 common small chain alcohol solvents; is that correct?

12 A. Yes. They both have those features in common.

13 Q. Methanol is a single carbon alcohol; is that correct?

14 A. Correct.

15 Q. And methanol is a two carbon alcohol?

16 A. That's right.

17 Q. In fact, sort of in order of alcohol it goes methanol,
18 ethanol, and then propanol; is that correct?

19 A. Correct.

20 Q. So the two smallest alcohols are methanol and ethanol?

21 A. Yes.

22 Q. And they have relatively similar solvent properties;
23 is that correct?

24 A. It depends what you mean by relatively similar. We're
25 back to the subjective words again, but they are different

Steed - cross

1 in their own way. Have different boiling points. Ethanol
2 is more lipophilic.

3 Q. Now, let us look at what is done in manufacturing the
4 form I and I want to make sure I use exactly the same
5 exhibit that was used before or whichever exhibit Ms.
6 Clayton wants me to use.

7 MR. SIPES: So, Ms. Clayton, is there a
8 particular exhibit that you would prefer me to pick up or
9 should I just -- I'm happy to use a different one if you
10 want or I just pull up JTX-573 and the question is do I need
11 to seal the courtroom?

12 MS. CLAYTON: JTX-573, is that the Sandoz one?

13 MS. SIPES: That's the close the courtroom one.
14 I will only look at the section that you looked at, but if
15 you want me to close the courtroom, I'm happy to do it.

16 MS. CLAYTON: No. I think if we just stick to
17 that one section we know that is already in Sandoz's
18 production, we don't need to close the courtroom.

19 MR. SIPES: I've been handed a note that may
20 help, too. I don't know that it's in the binder. So it is
21 in the binds err. Maybe in your direct binder, PTX-1407.
22 I'm told 1407 helps to avoid this problem.

23 MS. CLAYTON: It does.

24 MR. SIPES: Why don't we call up PTX-1407.

25 Then, you know what, go back to A and just focus on what we

Steed - cross

1 need to focus on, JTX-573. And I just want you to turn to
2 the second page at the top, just that. And I think we're
3 okay so far.

4 And let's blow up, if we will, the bottom row of
5 the synthesis, the bottom row, just so we understand what
6 we're talking about here.

7 BY MR. SIPES:

8 Q. So, to be clear, this is the manufacture of form I,
9 correct, that ultimately is in Sandoz's product; is that
10 correct?

11 A. That's my understanding.

12 Q. And as you say, the last step that makes ibrutinib is
13 the step that's labeled step 5 and the ibrutinib molecule is
14 then to the right of that and it's identified as ibrutinib
15 form E, is that correct, the toluene solvate?

16 A. Yes.

17 Q. And we're talking here form E. That's one of the
18 forms that is described in the '548 patent?

19 A. That's correct.

20 Q. The crystal lattice has ibrutinib and toluene in it?

21 A. Yes.

22 Q. Toluene is a fairly unpleasant compound. In fact,
23 cancer causing; is that correct?

24 A. No. I'm not sure I know that offhand. It's normally
25 used instead of benzene. I said I couldn't testify to it.

Steed - cross

1 Q. Okay. The point, you wouldn't want to use a toluene
2 solvate in a drug product if you could avoid it?

3 A. I guess so.

4 Q. But for whatever reason, they don't use form E and so
5 they've converted on; correct? They convert the crystalline
6 form away from form E?

7 A. Yes, that's right.

8 Q. Now, they don't take form E directly to form I.
9 There's an intermediate crystalline form; is that correct?

10 A. Yes, that's right.

11 Q. Now, you've not explained in your testimony why they
12 don't go straight from form E to form I; is that correct?

13 A. I can explain it if you would like. It's because
14 toluene is not mixed with water.

15 Q. So they have to take it to form, they take it to form
16 C first; is that correct?

17 A. Well, they re-crystallize it to get rid of its --

18 THE COURT: So there was a question. So they
19 have to take it to form, they have to take it to form C
20 first; is that correct?

21 And then the professor answered, well, they
22 re-crystallize it to get rid of its, and then we lost you.

23 THE WITNESS: Re-crystallize it to get rid of
24 its toluene.

25 THE COURT: All right. Sorry. Go ahead.

Steed - cross

1 BY MR. SIPES:

2 Q. Of course, there's no toluene in form A or B or form I
3 as well; correct?

4 A. That's my understanding.

5 Q. They're all unsolvated forms, so they have no solvents
6 of any kind; is that correct?

7 A. Correct.

8 Q. But the manufacturer decides to go to form C and then
9 take form C to form I; correct?

10 A. They do form C, yes. Methanol and toluene are mixed
11 with each other. They re-crystallize the solvent. They're
12 mixed with the toluene. They can filter that off and
13 redissolve it in the water.

14 Q. Then they take form C to form I using an ethanol water
15 mixture; is that correct?

16 A. It is using an ethanol water mixture. It's a
17 recrystallization step. Form C gets dissolved. All traces
18 of form C disappear and it gets re-crystallized as form I.

19 Q. Now, let's talk a little bit about -- we can take that
20 down now.

21 I think it was your testimony this morning that
22 to a person of ordinary skill in the art, it's routine to
23 distinguish one crystalline form from another once those
24 forms are known; correct?

25 A. Yes. You can compare X-ray powder diffraction

Steed - cross

1 patterns, for example.

2 Q. And so in terms of the analytic techniques to
3 determine whether or not a sample falls within claims 18 and
4 19, that would be routine to a POSA; correct?

5 A. I suppose, yes, it would be relatively routine to
6 simply take a sample, run a powder diffractogram, identify
7 what peaks are there. I assume you would have to do TGA to
8 determine whether it's solvated or not.

9 Q. And you might do solution NMR to confirm that it was
10 ibrutinib?

11 A. Yes.

12 Q. And are all of the techniques to determine whether a
13 sample falls within claim 18 and 19 are within the knowledge
14 of the POSA and can be carried out in a manner of a few
15 hours; is that correct?

16 A. You mean the characterization techniques?

17 Q. Correct.

18 A. Yes, depending on the amount of solid available, yes,
19 they're relatively fast. I guess not always so, but it
20 generally is.

21 Q. Now, let me ask you: Was your testimony this
22 afternoon that you can't, you don't think that one can claim
23 a genus of crystalline forms; correct?

24 A. Yes. The genus concept doesn't really make sense to
25 me in the context of those two forms.

Steed - cross

1 Q. Now, do you recall you were deposed in this case a few
2 months ago?

3 A. I do.

4 Q. And at your deposition, you testified, did you not,
5 that you certainly can claim more than one crystalline form
6 with a particular characteristic; is that correct?

7 A. Yes. But that's a little bit different, isn't it?
8 You could certainly, you could have a claim that says the
9 characteristic and then claim a different crystal form that
10 had that characteristic in common.

11 Q. In fact, it was your position, your testimony at
12 deposition that it was not your opinion that it is
13 impossible to claim crystalline forms of the genus?

14 A. Well, this genus concept is quite confusing.
15 Certainly, you can have more than one crystalline form with
16 a similar characteristic, PK in particular, but I wouldn't
17 characterize that as a genus. It's the characteristics of
18 individual crystal forms.

19 MS. CLAYTON: Your Honor, Mr. Sipes, can you
20 tell me what pages of his deposition transcript you are
21 referring to right now?

22 MR. SIPES: I can. In fact, let me see if I can
23 refresh his recollection on his testimony. We don't have to
24 play the clip. If we could pull up the transcript at page
25 138, line 16, through 139, 1.

Steed - cross

1 THE COURT: I'm kind of confused by the
2 objection. If you want to work it out, but there wasn't a
3 pending question. But maybe it was the delay because of the
4 remoteness or something, Ms. Clayton.

5 MS. CLAYTON: No. I was just wanting to know
6 what portions -- he keeps referring to the deposition. I
7 just wanted clarity on what portions of his deposition he
8 was referring to before he impeached him so I could make
9 sure it's proper impeachment.

10 THE COURT: Okay. But he answered yes to the
11 question.

12 MR. SIPES: Right. So it is not his position --
13 now he's saying you can call it a genus. A genus, that's
14 fine. I think you certainly claim more than one crystal
15 form of the particular characteristic and if you want to
16 call that a genus, then that's fine. That's our point. You
17 can, you can claim a genus. He had said you could not call
18 it a genus. He would not say it's a claimed genus.

19 THE COURT: Well, I mean, now we're in -- sorry.
20 This is part of the problem because it's remote. Now we're
21 just having attorney argument. Let's go back. I just want
22 to make sure.

23 What we've got is here --

24 MS. CLAYTON: I would say his original --

25 THE COURT: Wait. I'm not faulting any counsel.

Steed - cross

1 Maybe it's me. This is the problem with just we're all on
2 different continents or two of us are. Here's what I've got
3 in the record. And at your deposition, you testified, did
4 you not, that you certainly can claim more than one
5 crystalline form with a particular characteristic. Is that
6 correct?

7 Answer: Yes.

8 But that's a little bit different, isn't it?
9 You could certainly, you could have a claim that says the
10 characteristic and then claim a different crystal form that
11 had that characteristic in common.

12 "Question: In fact, it was your position, your
13 testimony at your deposition that it was not your opinion
14 that it is impossible to claim crystalline forms of the
15 genus.

16 "Answer: Well, this genus concepts is quite
17 confusing. Certainly, you can have more than one
18 crystalline form with a similar characteristic, PK in
19 particular, but I wouldn't characterize that as a genus.
20 It's the characteristic of individual crystal forms."

21 Okay. Now, at this point, I recognize Ms.
22 Clayton because she was standing and, again, because of the
23 delay, but there was no pending question.

24 So I'm going to let Mr. Sipes decide what you
25 want to do with that, sir. Okay?

Steed - cross

1 BY MR. SIPES:

2 Q. So at your deposition, you were fine with claiming
3 more than one crystalline form with the particular
4 characteristic and calling it a genus; correct?

5 THE WITNESS: You're mischaracterizing my
6 testimony. I said if you want to call that a genus, you
7 want to call that a genus, that's fine. I wouldn't call it
8 that. That's what it has been called to me. If that's, if
9 that's Ms. Bharkhda's definition of a genus, that's what I
10 meant by that comment. I wouldn't call it that.

11 MR. SIPES: Well, all right. Let's try then to
12 deal with it in terms of what is out there in the art. We
13 can take that down.

14 You're aware that Dr. Myerson in his rebuttal to
15 your opening report identified a number of patents in the
16 art, including patents from the defendant and defendants'
17 experts that specify and claim a group of crystalline forms
18 on the basis of a single 2-Theta peak; correct?

19 A. You'll have to refresh my memory.

20 Q. Why don't we look in your reply report at paragraph
21 116. So you say, Dr. Myerson also points to other patents
22 that recite a single 2-Theta peak.

23 Do you see that?

24 A. Yes.

25 Q. So do you recall Dr. Myerson identifying a number of

Steed - cross

1 patents in the art that specify and claim crystalline forms
2 on the basis of a single 2-Theta peak?

3 A. I didn't look at them in detail. As I said, I have
4 not analyzed these patents. I do recall him mentioning it,
5 but as I said, it's possible they have similar written
6 description problems. Single 2-Theta peak is not the way to
7 characterize crystalline form.

8 Q. In fact, you chose not to look at those patents;
9 correct?

10 A. Well, I kind of did everything, sir.

11 Q. And, in fact, you didn't analyze those patents because
12 you weren't asked to analyze them by counsel? Correct?

13 A. Yes, that's right. I don't doubt those claims are
14 missing things. Of course, when you are writing a patent
15 claim, you're trying to make it seem as normal as possible.
16 They are what they are. They may have written description
17 problems.

18 Q. So you chose just not to look at examples to try to
19 understand how other entities had found it appropriate to
20 claim a group of crystalline forms using none, one or two
21 crystalline forms; is that correct?

22 A. Well, as I said, I have not analyzed these patents in
23 detail, but to my knowledge, when people are drafting
24 patents, they try to make it as broad as possible.

25 Q. And that really comes maybe to the heart of what's

Steed - cross

1 going on here. In your view, should patent claims to
2 crystalline material always be limited to past forms, to
3 forms that have already been identified?

4 A. Well, patentability is a matter for the USPTO and it
5 varies according to jurisdiction and region.

6 THE COURT: Hold up, hold up. We've got an
7 objection.

8 MS. CLAYTON: The objection is it asks for a
9 legal conclusion, Your Honor. He's not a lawyer.

10 MR. SIPES: I'm asking his own opinion. Not his
11 legal opinion, his opinion giving what he's saying he thinks
12 it would ever be appropriate to claim crystalline forms that
13 have been beyond filing the patent at issue. He's
14 testifying about patents lacking written description and
15 enablement. He's opining on what is appropriate. I'd like
16 to find out if there are circumstances where he thinks you
17 can claim --

18 THE COURT: We are getting into legal argument
19 at some level. I will overrule the objection right now,
20 but I'm a little skeptical, so go ahead. Answer the
21 question.

22 THE WITNESS: Sir, I'm not a legal expert, but
23 my understanding is that a patent has to claim an invention
24 that's nonobvious, not anticipated and some way inventive.
25 So if claiming a crystal form fulfills those criteria, I

Steed - redirect

1 guess it would be patent able, but I would have to look at
2 the details of what is being claimed.

3 BY MR. SIPES:

4 Q. And in this case, you have not challenged the fact
5 that the crystalline ibrutinib that's described in the '548
6 patent is novel and nonobvious; is that correct?

7 A. I wasn't asked to form an obviousness opinion on the
8 patent.

9 Q. All right.

10 MR. SIPES: Your Honor, if I could just have a
11 moment to consult?

12 THE COURT: Sure. Yes.

13 MR. SIPES: Your Honor, I have no further
14 questions at this time.

15 THE COURT: Okay. Thank you, Mr. Sipes.

16 All right, Ms. Clayton. Any redirect?

17 MS. CLAYTON: Just actually one question, Your
18 Honor.

19 Sorry. One moment. Our tech person has to get
20 reconnected.

21 REDIRECT EXAMINATION

22 BY MS. CLAYTON:

23 Q. I might be able to ask the question without the
24 document. Dr. Steed, you recall the synthetic route for
25 form I that you were shown during your cross?

Steed - redirect

1 A. Yes.

2 Q. And do you -- Mr. Sipes asked you a number of
3 questions about seeding as well. Do you recall that?

4 A. Yes.

5 Q. Is there any evidence of seeding going on in the
6 synthetic route used to arrive at form I?

7 A. No, not at all.

8 MS. CLAYTON: I have no further questions Your
9 Honor.

10 THE COURT: All right. I have one question for
11 the professor.

12 All right. So if I look at the claim, let's
13 take 15, and it says, a crystalline form of one, and then it
14 has the formula, and then it says, that have an X-ray powder
15 diffraction, XRPD pattern comprising a 2-Theta peak at about
16 18.9, angstroms, I guess, right?

17 THE WITNESS: Degrees.

18 THE COURT: Degrees. Sorry. Okay. Is there
19 any document that you've been shown or that you have talked
20 about that would visually depict a 2-Theta peak at about
21 18.9 degrees? Could you just show me? In other words, is
22 it something like a layman like me, you could say, hey,
23 Judge, here's an XRPD pattern comprising a 2-Theta peak at
24 about 18.9 degrees.

25 THE WITNESS: Yes. You could look at the patent

Steed - redirect

1 itself, look at the 18.9 degrees and see if there's a peak
2 thereof.

3 THE COURT: Were you shown one today? I would
4 like to see one. I would like to know what it looks like,
5 you know, so I actually understand what we're talking about.

6 MR. SIPES: Your Honor, perhaps if we turn to
7 the '548 patent, JTX-1 at JTX-0001-00014. Can you pull that
8 up? Can we get control? There we go.

9 THE COURT: All right.

10 MS. CLAYTON: I they we have control. We can
11 pull it up, JTX.

12 Are you talking about Figure 1, Mr. Sipes?

13 MR. SIPES: Figure 1.

14 MS. CLAYTON: Yes.

15 THE COURT: Let him see that.

16 MR. SIPES: Yes. There we go.

17 If you want to blow up the central portion
18 there, that will make it easier to see where the peaks are.

19 THE COURT: Okay. So --

20 BY MR. SIPES:

21 Q. Dr. Steed, that tall peak right before what would be
22 19 on the scale, would that be a peak at 18.9?

23 A. Yes.

24 THE COURT: All right. So it has got one peak
25 there at about 18.9 degrees; is that correct?

Steed - redirect

1 THE WITNESS: Yes, sir.

2 THE COURT: I guess in layman's terms, and
3 maybe this is completely irrelevant, probably is, but since
4 I've got you here and, you know, what I am kind of confused
5 about is it seems undisputed that these XRPD's are the
6 analog of the fingerprint, although I think we've had some
7 testimony it's not a perfect analogy, but that there's some
8 there.

9 And what I'm confused about is, you know, we're
10 defining a pattern based on a single peak at a single degree
11 and I'm trying to figure out how that's helpful. In other
12 words, this seems like a complicated pattern and based on
13 other testimony and comparison of the XRPD pattern, it seems
14 to me there's more than just looking at a single peak or two
15 peaks or three peaks. I mean, and in this one, it looks
16 like there's a higher peak at, you know, four-and-a-half or
17 five degrees.

18 THE WITNESS: Right.

19 THE COURT: I will take the time on this. I'm
20 not going to punish the parties. Maybe I should. Can
21 somebody explain to me what this is all about? To a layman,
22 can you tell me how I read this chart? I've seen a lot of
23 fingerprint experts. They can explain to me how fingerprint
24 works. Can you explain how this data term, XRPD, works that
25 makes sense to me?

Steed - redirect

1 THE WITNESS: As I've described are, Your Honor,
2 one individual peak doesn't tell you very much at all. The
3 whole pattern of peaks is determined by the whole structure.
4 The whole structure is kind of encoded in the whole pattern,
5 but individual peaks don't correlate with individual
6 structure in the sense that there's information about the
7 whole structure in every peak. If you want to work
8 backwards, you get the whole pattern with the whole
9 structure.

10 THE COURT: Right. But we're saying that the
11 diffraction pattern has to comprise a peak.

12 THE WITNESS: It doesn't make a great deal of
13 sense to me.

14 THE COURT: Okay. And, counsel, either side are
15 free to ask a question. I'm sorry, but you can tell, I
16 mean, I'm ignorant about something, it seems pretty
17 fundamental. But I will leave it up to you. Mr. Sipes, do
18 you have any followup questions based on that?

19 MR. SIPES: No, Your Honor.

20 THE COURT: Ms. Clayton?

21 MS. CLAYTON: I will ask one.

22 BY MS. CLAYTON

23 Q. Is it possible -- strike that. So can you identify a
24 particular polymorphic form using only one peak?

25 A. No. It's the whole pattern.

Steed - redirect

1 Q. So does claiming a polymorphic form using a single
2 peak make sense in the science of XRPD?

3 A. No. The whole pattern really defines the form and
4 you're throwing away most of the information by just --

5 THE COURT: Okay. But what if the claim said it
6 is an XRPD pattern comprising ten Theta peaks? Would you
7 know what they are talking about at that point?

8 THE WITNESS: Yes. You could have a much better
9 chance, in defining the peaks, they were the ten strongest
10 peaks, for example.

11 MR. SIPES: Your Honor, I do have one followup.

12 THE COURT: Yes.

13 RECROSS EXAMINATION

14 BY MR. SIPES:

15 Q. When the identity of the compound is known, it is not
16 uncommon to use fewer characteristic peaks, whether it's
17 five or three or some number; correct?

18 A. Well, it depends on the nature of the experiment. If
19 you are doing qualitative Theta indication, which is what
20 the USP describes, then the whole pattern can be shortened
21 using ten peaks. If you know you've got one thing or the
22 other and one thing had a peak in a place and the other
23 doesn't, then you created a calibration just based on that
24 one peak. Completely different experiment.

25 Q. What you just referred to is Sandoz does what's called

Steed - redirect

1 a spiking experiment in which they put form A into form I
2 and they identify the presence of form A with just a single
3 peak; is that correct?

4 A. Yes, that's right. Very well defined experiment in
5 which two forms are present in the mixture and then you can
6 compare diffractograms based on the intensity of the peak
7 that correlated with how much you put in there. Under those
8 defined circumstances where you're not trying to identify
9 either peak, you're just trying to quantify how much is
10 there, you can use them.

11 Q. Depending on the context and the state of your
12 knowledge, you can use fewer peaks -- it just depends on
13 exactly what you are looking for.

14 A. You said use fewer peaks. In terms of identification,
15 no. If there's a spiking experiment, one peak. That's
16 about measuring how much material of a particular known
17 form is present, not identifying that known form.

18 THE COURT: All right. Thank you very much, I
19 appreciate your time. And have a good evening.

20 THE WITNESS: Thank you, Your Honor.

21 MR. SIPES: Thank you, Dr. Steed.

22 THE WITNESS: Thank you.

23 (Witness excused.)

24 THE COURT: All right. What's next?

25 MS. CLAYTON: So, Your Honor, at this point we

1 have some deposition testimony that we are going to play
2 from the inventors.

3 THE COURT: Wait. Okay.

4 MS. CLAYTON: Yes.

5 THE COURT: Incidentally, when you play -- I
6 don't know it's you, but when Alvogen played the inventor
7 testimony before, did you guys get together, both sides, to
8 figure out what the deposition would look like or was that
9 just the defendants playing? And the same question is going
10 to apply what you are about to play. Is this something that
11 was put together joint by the parties?

12 MR. SIPES: Yes. It includes designations and
13 counter-designations. I believe we submitted the clip
14 report that gives the time attributable to each party.

15 THE COURT: Okay. That's in the PTO, is it?
16 Clips.

17 MR. SIPES: It's in the binder.

18 THE COURT: Okay. I see many I was watching
19 them on the screen. All right. Thanks.

20 MS. CLAYTON: So, Your Honor, we'd like to
21 introduce the testimony of Mr. Erick Goldman. He is one of
22 the named inventors on both the '548 and the '231 patent.
23 He was designated a 30(b)(6) witness by plaintiffs for
24 certain topics.

25 There are 54 minutes and 47 seconds of his

1 deposition testimony. 38 minutes and 29 seconds will be
2 charged to the defendants and 15 minutes and 18 seconds will
3 be charged to plaintiffs.

4 THE COURT: Okay.

5 MS. BHARKHDA: Before we begin playing the
6 testimony, there is one issue that was crystallized by the
7 deposition clips that Sandoz wants to to play as well as the
8 opening slide, which are relevant to the testimony that will
9 be played and so if you would like to share that issue now,
10 we're happy to address it.

11 If you would like to put it off to later, we can
12 do that. I did want to let the --

13 THE COURT: Wait.

14 MS. BHARKHDA: -- the start of the deposition
15 play.

16 THE COURT: The ten second issue, what's the
17 issue about?

18 MS. BHARKHDA: The ten second version is that we
19 understand Sandoz to be pursuing here at trial several
20 improper inventorship theories.

21 I believe there are three improper inventorship
22 theories. One of those theories was not disclosed in
23 Sandoz's final contentions or in any expert reports. Sandoz
24 put it for the first time in the pretrial order. We
25 objected.

1 And so we are -- we have an interest with
2 respect to that theory and some of the testimony we believe
3 relates to that particular --

4 THE COURT: Yes. I do want to address it,
5 because I've got enough in my brain that I can only hold so
6 much and I don't want to be putting stuff in it that I don't
7 need to resolve. All right.

8 Why don't you quickly address that issue? Hold
9 on.

10 MS. CLAYTON: Sure.

11 THE COURT: Hold on. It came up in your
12 opening. Hold on. I want to get your opening slide so we
13 can talk through this.

14 MS. BHARKHDA: When it came up in the opening
15 slide, we flagged it as a dispute. Sandoz changed the
16 slide, but indicated they were still pursuing this theory.
17 So the issue remains, but I don't think the slides are
18 necessarily going to solve the problem.

19 THE COURT: Okay.

20 MS. BHARKHDA: I can point you to the relevant
21 portion of the PTO if that would be helpful.

22 THE COURT: Well, let's see. Maybe they're not
23 even pursuing it. Ms. Clayton?

24 MS. CLAYTON: So, Your Honor, I mean, to be
25 clear, we are pursuing that defense. So the specific

1 testimony they are objecting to though is testimony related
2 to what a company, Pharmorfix, did in discovering these
3 crystalline forms.

4 That testimony isn't solely relevant to the
5 inventorship issue. It needs to come in for 112 purposes,
6 too, and even Dr. Myerson in his rebuttal has cited to
7 documents from Pharmorfix that are talked about in the
8 inventor's deposition, and nine paragraphs of his rebuttal
9 report on invalidity where, as Mr. Bharkhda mentioned,
10 inventorship wasn't an issue.

11 So in our opinion, regardless of that objection,
12 the testimony about what Pharmorphix has done in connection
13 with these molecules should come in because it also shows
14 the extensive polymorph screening they did before the filing
15 date, which never resulted in anything other than A through
16 F.

17 So regardless of the inventorship issue, we
18 think that, you know, these are relevant and should be
19 played and come into the record.

20 THE COURT: Okay.

21 MS. CLAYTON: So I don't know if that resolves
22 this issue. I'm happy to address your argument that we have
23 not heard this first.

24 THE COURT: Let me hear the response.

25 MS. BHARKHDA: Your Honor, if Sandoz is

1 representing that they're going to be offering the testimony
2 for a different purpose, then I don't think we object to
3 them playing the testimony. It still leaves the unresolved
4 issue of the undisclosed theory which we believe the
5 testimony is actually being played for and we don't think
6 that the Court should be entertaining the theory because it
7 wasn't properly disclosed at any point before the filing of
8 the PTO.

9 THE COURT: Okay. So here's what we will do
10 then. Let's just play it. Your objections are noted and
11 you preserve your ability to preclude consideration for
12 admissibility of the evidence for, if it's used for
13 inventorship issues. Okay?

14 MS. BHARKHDA: Thank you, Your Honor.

15 THE COURT: That sounds good.

16 MR. HANNA: Your Honor, with respect to certain
17 designations that are about to be played, some of them are
18 for the crystalline patents. Alvogen's are in there as
19 well.

20 So, for example, we have Dr. Smyth, Phillip
21 Goldman. They would include designations for Alvogen as
22 well because those are the inventors on the '455 patent.

23 THE COURT: I'm sorry, Mr. Hanna. It has been a
24 long day. Basically, you and Sandoz, your designations are
25 for both of you is what you are saying?

Goldman - deposition designations

1 MR. HANNA: Yes.

2 THE COURT: All right. And then I don't have
3 the Goldman deposition designations, apparently, so we can't
4 find them.

5 MS. CLAYTON: We'll check on that, Your Honor.

6 THE COURT: We have the exhibits for Goldman,
7 but not the notebook with the deposition designations.
8 That's fine. I with watch them, but you probably want to
9 send that to us.

10 MS. CLAYTON: Yes. We'll make sure we do that,
11 Your Honor.

12 THE COURT: All right. Thanks.

13 (The videotaped deposition excerpt of Erick Alan
14 Goldman was played as follows.)

15 "Question: Good morning. Please state your
16 full name for the record.

17 "Answer: Erick Alan Goldman.

18 "Question: Now, when you started out at
19 Pharmacyclics, what were your responsibilities?

20 "Answer: Process chemistry.

21 "Question: And since you started at
22 Pharmacyclics in May of 2010 to now, can you estimate how
23 many projects you worked on at Pharmacyclics.

24 "Answer: Can you clarify what you mean by
25 projects?

Goldman - deposition designations

1 "Question: Sure. Separate development --
2 of a certain -- well, put it this way. At Pharmacyclics, do
3 they -- when they develop a certain drug or -- do they call
4 it a project?

5 "Answer: Sure.

6 "Question: Okay. That's what I mean by
7 projects.

8 "Answer: So for separate drug targets?

9 "Question: Yes.

10 "Answer: -- I have worked on -- give me a
11 minute here.

12 "Question: Sure.

13 "Answer: Could I ask for one clarifying
14 question.

15 "Anser: So technically,, I worked on several
16 projects that didn't advance very far, so I guess I will
17 ask, to what level of progress are you specifically asking
18 about for these compound?

19 "Question. Well, let me clarify. I appreciate
20 that. I'm asking about all projects, whether they
21 progressed very far or not, and I'm also just asking for an
22 estimation. I'm not asking for, like, a specific number.

23 It seems like that might give you --

24 "Answer: That's what -- that's really tough.

25 "Question: Why don't I --

Goldman - deposition designations

1 "Answer: Well, over 20.

2 "Question: Now, the ones that actually
3 progressed to a further development stage, how many projects
4 -- estimate -- have you worked on?

5 "Answer: Over ten.

6 "Question. Okay. Out of those ten that you're
7 thinking of --

8 "Answer: Again, it's an estimate, how many
9 involved working with polymorphic forms of the compound --
10 compounds?

11 "Answer of. Most of them.

12 "Question: Okay. Is there a particular reason
13 why most of them would have been involving polymorphic forms
14 of compounds?

15 "Answer: Okay. So the particular stage of
16 development that I'm discussing for -- for these over ten
17 compounds that I mentioned, those are all, those were all on
18 track for clinical candidacy, so it's important to
19 understand the polymorphic landscape of those compounds
20 going into -- to IND-enabling activities.

21 "Question: Why is it important to understand
22 polymorphic compound?

23 "Answer: To establish control.

24 "Question: Is part of it because you need to
25 report to the FDA that information?

Goldman - deposition designations

1 "Answer: That's part of it.

2 "Question: Okay. Is there any other reasons?

3 "Answer: Yes. There are -- there are quite a
4 few.

5 "Question: Okay. Any come to mind right now?

6 "Answer: As I had mentioned, control is very,
7 very important. So it's very, very critical to understand
8 not only what you previously obtained, but what you expect
9 to obtain in developing a pharmaceutical route.

10 "Question: Now, you're aware that this case
11 involves ibrutinib; correct?

12 "Answer: Sure.

13 "Question. And at Pharmacyclics, was that
14 referred to as a kinase project? Is that accurate?

15 "Answer: Yes.

16 "Question: All right. And when did you start
17 working on the kinase project?

18 "Answer. For this specific kinase project?

19 "Question: At Pharmacyclics. Correct?

20 "Answer: For ibrutinib, I started working in
21 2010 at some point in time.

22 "Question: I'm actually just generally asking
23 if you -- I'm generally asking what your responsibilities
24 were when you started, if you could list them, what comes to
25 mind.

Goldman - deposition designations

1 "Answer: So impurity generation was part of
2 them. Testing samples of critical starting materials,
3 different lots, that was a big one. And -- and then getting
4 involved, yes, with the polymorph studies.

5 "Question: Okay. What has been handed you
6 has been marked deposition Goldman deposition Exhibit 3.
7 It's -- on the front of it, it says U.S. Patent 9,296,753
8 and I has Bates numbers IMBPCYC04446077 through 141.

9 "Do you have that document in front of you?

10 "Answer: I do.

11 "Question: Okay. Are you familiar with this
12 patent?

13 "Answer: Yes, I am.

14 "Question: Okay. And if you look at the page
15 that you're looking at, the second page. There's a list of
16 inventors and the second name is Erick Goldman. That's you.

17 "Answer: That is me.

18 "Question: Okay. Can you tell me generally,
19 what's your contribution to this patent?

20 "Answer: My general contribution would be
21 directing research and conducting experiments that help lead
22 to the elucidation of crystal forms as well as exploration
23 of others.

24 "Question: And when you mean others, you mean
25 other crystal forms?

Goldman - deposition designations

1 "Answer: Other crystal forms.

2 "Question: Other crystal forms not in this
3 patent? What -- sorry. Let me clarify. What do you mean
4 by others?

5 "Answer: What I meant by others was in addition
6 to what under -- what had already been found prior to my
7 arrival at Pharmacyclics.

8 "Question: Prior to your arrival at
9 Pharmacyclics, what polymorphic forms of ibrutinib were
10 known?

11 (Reporter requested clarification.)

12 "THE WITNESS: Form A, form B, and form C.

13 "Question: Now, the inventors, it lists Mark
14 Smyth. You referred to him already. Correct?

15 "Answer: Correct.

16 "Question: What was his contribution to this
17 patent?

18 "Answer: He was in charge of process chemistry
19 and the ibrutinib project, specifically anything related to
20 the chemistry of ibrutinib.

21 "Question: And there's David Wirth. That's the
22 third name. Do you see that?

23 "Answer: Uh-huh.

24 "Question: What was his contribution to this
25 the patent?

Goldman - deposition designations

1 "Answer: David Wirth, his research at Ceres
2 Laboratories led to the initial isolation of crystalline
3 forms of ibrutinib.

4 "Question: And the last person is Norbert
5 Purro. What was his contribution to this patent?

6 "Answer: He is the one who formulated various
7 crystal forms.

8 "Question: And for the kinase project, did you
9 have any involvement with the formulation of the product
10 that's sold at Imbruvica?

11 "Answer: Outside of providing the crystalline
12 API that was used for the formulation, no, I did not.

13 "Question: Have you had any involvement with
14 coming up with the formulation using ibrutinib?

15 "Answer: Same answer: Outside of providing the
16 API, no.

17 "Question: Okay. Let me direct your attention
18 to column 63. Do you see the columns at the top, numbers?

19 "Answer: All right.

20 "Question: And specifically, I'm going down to
21 Example 1 there. Do you see that?

22 "Answer: I do.

23 "Question: Okay. And it says, "The
24 preparation of crystalline forms of, then it has a chemical
25 compound.

Goldman - deposition designations

1 "That chemical compound, that's ibrutinib.

2 Correct?

3 "Answer: Yes, it is.

4 "Question: And if you go from column 63 to 64,
5 there's form A, and there's Route 1, Route 2, Route 3.

6 "Do you see those?

7 "Answer: I do.

8 "Question: Okay. And then it continues to go
9 down, and you see form B and then form C, form D. And then
10 if you turn the page, there's form E and form F.

11 "Do you see that?

12 "Answer: I do.

13 "Question: Okay. So these are the different
14 polymorphic forms for ibrutinib. Correct?

15 "Answer: These are the ones described in this
16 patent.

17 "Question: Okay. Are there additional ones?

18 "Answer: Sure.

19 "Question: Okay. But they're not described in
20 this patent?

21 "Answer: Not in this patent specifically, no.

22 "Question: Okay. What's been handed to you has
23 been marked Goldman Exhibit number 5. It has Bates numbers
24 IMBPCYC05392658 to 59. At the top it says kinase project
25 team meeting minutes, 10/30/2007.

Goldman - deposition designations

1 "Do you have that in front of you?

2 "Answer: I do.

3 "Question: Okay. Now, I want to go down to the
4 last bullet on the first page. And you see 32765 solid form
5 (Erick, Alice, Greg, and Lee).

6 "Do you see that?

7 "Answer: I do.

8 "Question: And 32765, again, that's ibrutinib?
9 Correct?

10 "Answer: Correct.

11 "Question: Sure. First of all, just -- do you
12 see the first sentence there where they're talking about
13 contract lab SSCI?

14 "Answer. I do see that.

15 "Question: Pharmacyclics did end up contracting
16 with SSCI to investigate polymorphs. Is that correct?

17 "Answer: That's accurate.

18 "Question: Do you know why Pharmacyclics was
19 investigating polymorphic forms of ibrutinib at this time,
20 2007?

21 "Answer: My understanding at the time is that
22 they were preparing for IND submission mid-2008, I believe.
23 And so it was -- per typical protocol, we wanted to
24 understand -- they wanted to understand the polymorphic
25 landscape a little bit as well as for purification, you

Goldman - deposition designations

1 know, processing and other benefits to a would be synthetic
2 process.

3 "Question: If you look at the document, the
4 third light bullet down, it says:

5 "In order to meet a June IND goal, we plan to
6 develop PCI-32765 as a free base.

7 "Is this consistent with your understanding that
8 they were looking into polymorph forms because they were
9 preparing an IND?

10 "Answer: That's correct.

11 "Question: What has been handed to you has been
12 marked Goldman deposition number 6. It has Bates number
13 IMBPCYC 05547529.

14 (Reporter requested clarification.)

15 "Question: Do you have that document in front
16 of you?

17 "Answer: I do.

18 "Question. Okay. It says Aptuit.com. Aptuit,
19 is your understanding Aptuit is SSCI?

20 "Answer: That would be consistent.

21 "Question. Okay. And this is consistent with
22 your understanding that Pharmacyclics used SSCI to do a
23 polymorph screen about 2008 time frame. Is that right?

24 "Answer: That is consistent with my
25 understanding, yes.

Goldman - deposition designations

1 "Question: And this would be the sample being
2 shipped to them to do that polymorph screen; correct?

3 "Answer. It looks like Mark was planning on
4 sending them some material, yes.

5 "Question: And the sample is labeled PIPR
6 203-R. Is that right?

7 "Answer: Correct.

8 "Question: What's been handed to you has been
9 marked Goldman Exhibit No. 8, Bates numbers IMBPCYC05450807
10 to 965. There's a letter on the front that says July 21st,
11 2008, to Mark Smyth from David Engers, and it identifies
12 SSCI at the top.

13 "Do you have that document in front of you?

14 "Answer: I do.

15 "Question: And you see SSCI says, underneath,
16 an Aptuit Company.

17 "Answer: That's what it says, absolutely.

18 "Question: So it's consistent with your
19 understanding that there's a relationship between the two;
20 correct?

21 "Answer: Yes.

22 "Question: Do you recognize this document at
23 all?

24 "Answer: I have not seen this document in its
25 entirety before. I have seen some parts, but not -- not

Goldman - deposition designations

1 this entire document.

2 "Question: Okay. But you're familiar -- well,
3 if you go to the next page, it's the first page of the
4 actual report. It has a date, said report generated for
5 Pharmacyclics on 7/18/2008.

6 Do you see that?

7 "Answer: I do.

8 "Question: So you're familiar that
9 Pharmacyclics had SSCI conduct a polymorph screen around
10 that time, 2008. Correct?

11 "Answer: Yes.

12 "Question: All right. And just if you go to
13 page 9 of the report, do you see the results and discussions
14 section?

15 "Answer: I do see that.

16 "Question: All right. In fact, if you go up to
17 the introduction, you see that in the second paragraph, the
18 second page, it says:

19 "For the Study 2 samples, lots PIPR-203-R and
20 PIPR-203 were received from Pharmacyclics and partially
21 characterized.

22 "Do you see that?

23 "Answer: I do.

24 "Question: Okay. So the samples that were sent
25 to SSCI were indeed PIPR-203R and PIPR-203. Right?

Goldman - deposition designations

1 "Answer: According to this introduction, yes.

2 "Question: And so the Route 3, do you know who
3 conducted that recrystallization?

4 "Answer: I don't recall for sure.

5 "Question: Okay. Do you know who would know at
6 Pharmacyclics?

7 "Answer: Not specifically, no.

8 "Question: Okay. And do you know whether that
9 recrystallization was done at Pharmacyclics or done by an
10 outside manufacturer?

11 "Answer: I don't recall.

12 "Question: And how good is melting point to
13 determine what polymorphic forms you have?

14 "Answer: Melting points is -- it is similar to
15 DSC.

16 "Question: DSC.

17 Well, is XRD a better technique to determine
18 what type of polymorph the compound is?

19 "Answer: From my experience, XRPD is preferred.

20 "Question: Do you know who came up with the
21 acetone heptane/recrystallization?

22 "Answer: My understanding is David Wirth did.

23 "Question: And he's at Ceres?

24 "Answer: He was the scientist at Ceres.

25 "Question: Okay. And do you know why that

Goldman - deposition designations

1 recrystallization was chosen?

2 "Answer: Again, my understanding -- not being
3 there, I can't say definitively -- but my understanding is
4 this is the crystal form setting slurry. This is the one
5 that consistently produce form A.

6 "Question: Okay. Well, and so we went over a
7 2008 SSCI polymorph screen. Right? We talked about that
8 earlier. Correct?

9 "Answer: Sure.

10 "Question: After the SSCI polymorph screen,
11 Pharmacyclics did another polymorph screen done by a company
12 called Pharmorphix; is that right?

13 "Answer: Pharmorphix.

14 "Question: Pharmorphix. Is that right?

15 "Answer: That is correct.

16 "Question: And now that screen was done when
17 you had -- after you had started at Pharmacyclics. Correct?

18 "Answer: Correct.

19 "Question: Okay. Were you involved with that
20 polymorph screen done by Pharm -- I'm going to screw that up
21 all day long now. Pharmorfix, Pharmorphix?

22 "Answer: Pharmorphix.

23 "Question. Let me try again. Sorry.

24 "Are you -- were you involved with the polymorph
25 screen done by Pharmorphix?

Goldman - deposition designations

1 "Answer: Yes, I was.

2 "Question: What's been handed to you has been
3 marked Goldman Exhibit No. 9. It has got Bates numbers
4 IMBPCYC05277895, and it's an e-mail. At the top it says,
5 from Mark Smyth and to Theirry Bonnaud, and it's dated
6 May 24th, 2011.

7 Do you have that in front of you?

8 A. I do.

9 "Question: Okay. And it says, samples for
10 P-1872. Do you see that?

11 "Answer: I do see that.

12 "Question: All right. Is that referring --
13 P-1872, does that refer to the polymorph screen that
14 Pharmorphix did for Pharmacyclics?

15 "Answer: That's accurate.

16 "Question: Okay. And it's discussing a
17 shipment of a sample. To your understanding, is this the
18 shipment of ibrutinib that was going to be used in that
19 polymorph screen?

20 "Answer: So multiple samples were sent for
21 purposes of the screen.

22 "Question: Okay. And the e-mail is describing
23 that. Correct?

24 "Answer: Yes.

25 "Question: And you were cc'd on the e-mail.

Goldman - deposition designations

1 Correct?

2 "Answer: I am.

3 "Question: Okay. Now, Pharmorphix -- why did
4 Pharmacyclics choose them to run the polymorph study?

5 "Answer: I had run a few projects with them in
6 my previous employment and liked their work. Their -- if I
7 recall correctly, other folks at Pharmacyclics were familiar
8 with them as well.

9 "Question: So you had input into the decision
10 to use Pharmorphix for the polymorph study?

11 "Answer: I did.

12 "Question: And who else had input into that
13 decision?

14 "Answer: Mark.

15 "Question: Dr. Smyth?

16 "Answer: Dr. Smyth, yes.

17 "Question: Okay. How much experience did they
18 have in conducting the polymorph screens at the time this
19 was done in 2011?

20 "Answer: They are considered to be experts in
21 the field of solid state chemistry.

22 "Question: They're a company in -- as a
23 company, by 2011, they were regularly conducting polymorph
24 screens. Is that -- is that accurate?

25 "Answer: That is accurate.

Goldman - deposition designations

1 "Question: What's been handed to you has been
2 marked as Goldman deposition Exhibit No. 10. It says Bates
3 numbers IMBPCYC05252966 to 3037.

4 "Do you recognize this document at all?

5 "Answer: Yes, I do.

6 "Question: Okay. Is this the report from the
7 Pharmorphix on the polymorph study that they conducted for
8 Pharmacyclics?

9 "Answer: Yes, it is.

10 "Question: Okay. And on the front, it's signed
11 and dated February 28, 2012, and one is February 30th, 2012.

12 "Does this report issue on or about that time?

13 "Answer: This was approved on that time, yes.

14 "Question: Well, actually, the report was
15 received -- does it comport with your understanding that the
16 report was received around February 2012?

17 "Answer: At Pharmacyclics?

18 "Question: Yes.

19 "Answer: Yes.

20 "Question: Okay. When it was received at
21 Pharmacyclics, did you review -- did you review the report?

22 "Answer: Yes.

23 "Question: Okay. And then if you go to the
24 next page, there's a Section 7.2, and it's initial
25 polymorphism screen.

Goldman - deposition designations

1 Do you see that?

2 "Answer: Yes.

3 "Question: And that is the initial -- that is
4 one of the polymorph screens that Pharmorphix did for
5 Pharmacyclics for this project. Right?

6 "Answer: Correct.

7 "Question: If you look at the next page,
8 there's a table 7, and it has a whole series of conditions
9 for the polymorph screens.

10 Do you see that?

11 "Answer: I do see that.

12 "Question: Okay. So there's a table, and
13 there's a list of solvents.

14 "Did Pharmorphix propose what solvents to use in
15 this polymorph screen?

16 "Answer: Pharmorphix provided an initial list,
17 and PCYC -- sorry, Pharmacyclics collaborated with
18 Pharmorphix to fine-tune the list a little bit.

19 "Question: What was the fine-tuning that was
20 done?

21 "Answer: Some solvents were removed; some were
22 added.

23 "Question: Do you know how those solvents were
24 chosen?

25 "Answer: I can state that for some of them,

Goldman - deposition designations

1 they were chosen based on their inclusion already in the
2 existing process.

3 In some cases, they were chosen because they
4 were considered to be Class 3 solvents, which means you can
5 have higher residual tolerance in your API, meaning --
6 meaning you don't have to get it down to ppm levels on -- in
7 terms of -- all API's have residual solvents, so there's a
8 little bit more tolerance with Class 3 solvents. So that's
9 why some of those are used in final IPPI isolations.

10 And a couple of the conditions were known to
11 purify the material.

12 Question. Well, your experience with -- with
13 working with polymorphs up to this point, 2012, were these
14 solvents common solvents that you'd use for a polymorph
15 screen?

16 "Answer: Can you give me your definition of
17 common, please?

18 "Question. You used -- used typically in
19 polymorph screen?

20 "Answer: As I stated earlier, some of them
21 would be used based on their Class 3 characteristics.
22 Others you will see -- you will include or not include based
23 on what you know about the molecule itself, so that would
24 not be typical.

25 "Question: Okay. But the ones that proposed

Goldman - deposition designations

1 that Pharmorfix proposed, do you know how they chose those
2 particular solvents to use:

3 "Answer. I don't, actually.

4 "Question: Okay. What's been marked as Goldman
5 deposition Exhibit 11, it got Bates numbers IMBPCYC05199288
6 and to -- to 298. And it says on the front page,
7 polymorphism studies on PCI-32765-00. Update 001.

8 "Do you have that in front of you?

9 "Answer: I do.

10 "Question: Okay. Did Pharmorfix give
11 Pharmacyclics periodically updates, presentations?

12 "Answer: They did.

13 "Question: Okay. And there's a Craig Boyle on
14 the front page. Who is Craig Boyle?

15 "Answer: Craig was a scientist who was
16 conducting a fair share of these experiments.

17 "Question: Okay. And would you review these
18 updates?

19 "Answer: I don't know if I received them -- I
20 don't recall if I received them directly, but I did have the
21 opportunity to review them.

22 "Question: And does this look like one of the
23 updates that Pharmorphix would give to Pharmacyclics on the
24 polymorph study?

25 "Answer: Yes, it is.

Goldman - deposition designations

1 "Question: On the front page, there's a date,
2 May 6, 2011. Does that comport with about the time when
3 Pharmorphix was starting this polymorph screen?

4 "Answer: It's in the time frame.

5 "Question: Okay. And it says update 001. So
6 this would have been the first update. Right?

7 "Answer: I think that's safe to assume, yes.

8 "Question: So if you direct your attention to
9 page 3, the slide 3 of the update, do you see that? It
10 says, "proposal" at the top?

11 "Answer: Yes, I'm sorry. I was trying to find
12 where the number was. Here we go. Yes, I see it.

13 "Question: So it says proposal at the top.
14 Right?

15 "Answer: Uh-huh.

16 "Question: So this summarizes the proposal that
17 Pharmorfix had for this polymorph screen. Correct?

18 "Answer: Yeah, but this was honed from the
19 original proposal. So the original proposal received was
20 fine tuned between Pharmacyclics and Pharmorphix.

21 "Question: Okay. Okay. Well, let me go back
22 to the report.

23 "Answer: Okay.

24 "Question: It's Exhibit 10. All right? And
25 I'm -- again, I'm on the initial polymorph screen. So it's

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1 page 24 of the report.

2 "Answer: Okay.

3 "Question: Okay. And if you look at the next
4 page, which is Table 7, it reports XRP data.

5 Do you see that? Or it has a column for XRPD.
6 Sorry.

7 "Answer: Which column?

8 "Question: It's the second to the right.

9 "Answer: Okay.

10 "Question: So you see it's XRPD after slow
11 cooling to zero degrees. Right?

12 "Answer: Yes.

13 "Question. And that reports the form underneath
14 the column. Right?

15 "Answer: Correct.

16 "Question: Okay. And to the best of your
17 understanding, that is the form that was obtained from this
18 polymorph screen. Is that right?

19 "Answer: To the best of my knowledge, yes.

20 "Question: Okay. And if you could go to
21 Exhibit 3, right -- it's the patent, sorry. It's the
22 patent. And let's go to column 63. All right?

23 And I'm looking at the Example 1 again. Answer:
24 Okay.

25 "Question: And it's form A, and now I'm looking

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1 at Route one. Do you see that?

2 "Answer: I do.

3 "Question: Okay. Does that Route one
4 correspond with this polymorph screen that we just discussed
5 on page 24 and 25 of the Pharmacyclics -- sorry, Pharmorphix
6 screen report?

7 "Answer: If you'll give me a minute.

8 "Question: Sure.

9 "Answer: They do appear to correspond.

10 "Question: And did you separately run
11 experiments that are described in Route one of the patent?

12 "Answer. I don't remember if I ran these exact
13 procedures or not.

14 "Question: Do you --

15 "Answer: -- in house.

16 "Question: Sorry. Do you remember if anyone
17 ever at Pharmacyclics ran those procedures?

18 "Answer: I don't recall.

19 "Question: Let's go back to the polymorph
20 screen that's Exhibit 10. I think you're on the right page,
21 25.

22 "Answer: I have page 25.

23 "Question. All right. 7.3, maturation screen.
24 Do you see that section?

25 "Answer: I do.

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1 "Question: Okay. And it goes to Table eight.

2 It's the next page, which describes the result of the

3 maturation; correct?

4 "Answer. That is correct.

5 "Question: All right. Now, on page 26, did

6 Pharmorphix propose the solvents to be used in this

7 maturation screen?

8 "Answer: So similar to my answer before, this

9 list appears to be the same as the initial polymorph

10 screening list, if I'm not mistaking, which means that it

11 was a collaborative list between Pharmorphix and

12 Pharmacyclics.

13 "Question: And the procedure on page 25,

14 there's a procedure for the maturation screen.

15 "Do you see that?

16 "Answer: I do.

17 "Question. Okay. Did Pharmorphix propose this

18 procedure for the maturation screen?

19 "Answer: I don't recall that Pharmacyclics had

20 any input on this procedure.

21 "Question: Okay. Do you know one way or the

22 other?

23 "Answer: One way or the other --

24 "Question. Oh. You just don't recall --

25 "Answer: I don't recall.

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1 "Question: And you don't recall that
2 Pharmacyclics had any input into the procedure. Correct?

3 "Answer: I don't recall.

4 "Question: Okay. Let's go back to the patent.

5 "Answer: Okay.

6 "Question: Which is in Exhibit Number 3, and
7 that same page we've been looking at; the column 63 -- now
8 this -- and I'm looking at form A, Route 2. Do you see
9 that?

10 "Answer: Okay.

11 "Question: Is Route 2 the maturation screen
12 that was conducted by Pharmorfix for the polymorph screen
13 that Pharmacyclics had them conduct?

14 "Answer. Route 2 from the patent appears to be
15 consistent with the maturation screen that you just
16 described for Pharmorphix.

17 "Question: Look in the front. There are some
18 figures. They start at -- they start at Figure 1, and the
19 Bates number is 4,446,085.

20 "Answer: Okay.

21 "Question: Do you see that?

22 "Answer: I do.

23 "Question: Okay. And it says XRPD pattern of
24 form A.

25 "Do you see that?

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1 "Answer: I do.

2 "Question: Okay. And do you know who -- where
3 that data came from?

4 "Answer: I believe this data came from
5 Pharmorfix.

6 "Question: And -- but you don't know what -- do
7 you know a way to be able to link up this particular data
8 with what sample that it came from?

9 "Answer: Pharmorphix sent us data to be
10 included in this. I don't recall if the lot numbers were
11 listed on that data or not.

12 "Question: Were you involved with sending that
13 data?

14 "Answer: Sending?

15 "Question: Giving it over so that it could be
16 put inside the patent application Dr. Hsu. Right. And
17 that's not what I'm trying to get to. I just --

18 THE WITNESS: Yeah, I believe I gathered
19 information from Pharmorphix and provided it to the IP
20 attorneys.

21 "Question: Now, we were previously talking
22 about the 2008 SSCI polymorph screen that was done for farm;
23 right?

24 "Answer: No.

25 "Question: And we also discussed the

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1 Pharmorphix polymorph screen that was done for
2 Pharmacyclics; correct?

3 "Answer: Yes.

4 "Question: Okay. And that was done about 2011,
5 2012, correct?

6 "Answer: The Pharmorfix screen was 2011.

7 Question. Correct.

8 "Answer: -- was 2011. Initiated 2011.

9 "Question: And the report was issued 2012.
10 Correct?

11 "Answer: This report was issued 2012, yes.

12 "Question: So between the 2008 SSCI polymorph
13 screen and the 2011 Pharmorfix polymer screen, did
14 Pharmacyclics conduct any other polymorph screens?

15 "Answer: Between those two reports?

16 "Question: Yes.

17 "Answer -- and projects?

18 "Question: Yes.

19 "Answer: So part of the time predates my
20 arrival of Pharmacyclics. Let's be clear about that.

21 "Question: Yes.

22 "Answer: I don't recall any.

23 "Question: Not that you're aware of?

24 "Answer: No. That's okay. Yeah. Not none
25 that I'm aware of.

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1 "Question: If we go back to the Pharmacyclics
2 polymorph screen that's Exhibit 10 in their report, was
3 David Wirth involved with this polymorph screen that was run
4 by Pharmorphix?

5 "Answer: No, he was not.

6 "Question: So that's the extent of your
7 involvement in the formulation development. You helped
8 provide the API; is that correct?

9 "Answer: That is correct.

10 "Question: What has been handed to you has been
11 mark Goldman Deposition Exhibit 14. It has Bates numbers
12 IMBPCY05000693 to 9849.

13 "And, again, I'm going to ask you -- the third
14 page in, it says, assigned to and then Erick Goldman.
15 That's you.

16 "Answer: Correct.

17 "Question: And it's dated assigned, this one is
18 clear, August 1?

19 "Answer: Correct.

20 "Question: I just want to be clear, does this
21 appear?

22 "Answer: Again, from a request.

23 "Question: A document the with the Bates
24 labeled IMBPCY04446822.

25 "I will turn you over to the second page,

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1 Mr. Goldman. Are you on the second page?

2 "Answer: I am.

3 "Question: This is the '549 patent. Right?

4 "Answer: Yes.

5 "Question: What did Pharmacyclics make its
6 first ibrutinib solvate?

7 "Answer: My understanding is that the first
8 solvate was characterized during the initial Pharmorfix
9 polymorph screen.

10 "Question: And the date of that was?

11 "Answer: I believe we established that was
12 somewhere along the lines of mid-2011 through the end of the
13 year 2012.

14 "Question: Did Pharmacyclics make a solvate
15 using free base ibrutinib or a pharmaceutically acceptable
16 salt of ibrutinib using any of these solvents listed here?

17 "Answer: Yes.

18 "Question: Which solvent was used?

19 "Answer: So the ones I recall are toluene,
20 methylethyl ketone and methanol.

21 "Question: Anything else?

22 "Answer: During the time frame that you were
23 you --

24 "Question. Ever.

25 "Answer: Ever. Okay.

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1 There are others, but I don't remember which
2 ones they had were off the top of my head.

3 "Question: The first polymorphic screening
4 assay, that was done by SCI; is that correct?

5 "Answer: With regards to ibrutinib.

6 "Question: Correct.

7 "Answer. To the best of my knowledge, yes, the
8 first polymorphic screen on ibrutinib was performed by SSCI.

9 "Question: And about four years later,
10 polymorphics goes on a second screening effort?

11 "Answers: Polymorphics. Thank you.

12 Do you know why Pharmacyclics decided to do more
13 polymorphics screening four years later?

14 "Answer: To continue to research their API.

15 "Question: Was there anything inadequate or
16 inconclusive about the first screening effort by SSCI?

17 "Answer: I don't know as I was not there at the
18 time. I would say the effort was more along the lines just
19 to be thorough.

20 "Question: Do you know if it had anything to do
21 with the anticipated filing of an NDA?

22 "Answer: So an NDA is always the goal. Right?
23 But being familiar with the API to get to that goal is more
24 of a step than I would say a pathway.

25 "Question: What do you mean by, it's a step?

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1 "Answer: It's just part of the development of
2 your API.

3 "Question: If you could turn back to
4 Exhibit 10.

5 "Are the solvents here Class 3 solvent? Table
6 7?

7 "Answer: No, they are not.

8 "Question: Is there a listing that the FDA
9 has or somebody has that identifies what falls within Class
10 3?

11 "Answer: Yes, there is.

12 "Question. Handing you Exhibit 21.

13 "Answer: Okay.

14 "Question: Is that an e-mail from you dated
15 August 25th, 2012, and an attachment thereto?

16 "Answer: Yes, it appears to be.

17 "Question: The attachment all has the same
18 Bates number, it looks like.

19 "My question was: Do you know with a that slide
20 deck concerns?

21 "Answer: Yes, I do.

22 "Question: What?

23 "Answer. It is a presentation that I assembled
24 describing some of the research I did in-house.

25 "Question: If you could turn to slide 3, which

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1 is 450 on the top Bates number.

2 "Answer: Okay.

3 "Question: Under the first heading, it says,
4 forms and conditions that derive them.

5 "Do you see that?

6 "Answer: I do.

7 "Question: And it says, form C is typically
8 isolated neat methanol. Is that correct?

9 "Answer: That is.

10 "Question: And form B is typically isolated at
11 room temp or cooler from aqueous methanol; is that correct?

12 "Answer: That is correct.

13 "Question: And form A is found in just about
14 any solvent matrix not containing methanol, asterisk. Is
15 that correct?

16 "Answer. That is what's written there.

17 "Question: And the asterisk is indicating there
18 that metastable MIB K and toluene solvates were two solvents
19 that did not yield form A. Is that correct?

20 Answer: Yeah, that -- so it just -- it says,
21 metastable MIB K and toluene solvates accepted.

22 "Question: What does that mean?

23 "Answer: I believe at the time I was referring
24 to the Pharmorphix report.

25 "Question: And those were two solvents that

Goldman - deposition designations

1 didn't yield form A?

2 "Answer: No. Those were the solvates that
3 Pharmorphix found.

4 "Question: You're aware that the patents that
5 we have looked at today describe the form A through. If of
6 ibrutinib. Correct?

7 "Answer: I am aware of that, yes.

8 "Question: Are you aware of any other forms of
9 form A through F at ibrutinib?

10 "Answer: Yes, I am.

11 "Question: How are you aware of those forms?

12 "Answer: Let's see. Through research that was
13 conducted at Pharmorphix under our direction at
14 Pharmacyclics.

15 "Question: Is there -- do you know if there's a
16 general or accepted rule of thumb as to how many peaks in an
17 XRPD spec you need to look at in order to identify a
18 particular polymorph versus another one?

19 "Answer: I don't know of a set standard.

20 "Question: Do you have a personal practice?

21 "Answer: With regards to a number of peaks?

22 "Question: Yeah. How many you would want to
23 focus -- or would need to consider or identify in a pattern
24 to conclude that it is, in fact, the same polymorphic form?

25 "Answer: That would be done on a case-by-case

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1 basis depending upon the compound itself.

2 "Question. Okay. How about for ibrutinib?

3 "Answer: I personally don't have a second
4 number of peaks that I put, put forth.

5 "Question: Do you believe you could identify a
6 polymorphic form with a -- of ibrutinib using just one
7 peak?

8 "Answer: No.

9 "Question: How about two peaks?

10 "Answer: No.

11 "Question: How about three peaks? And that
12 will be the last one.

13 "Answer: No.

14 "Question: If you could pull out the '753
15 patent for me, which I think is Exhibit 3.

16 "Answer: Okay.

17 "Question: I think we've established multiple
18 times today that this patent references the crystalline
19 forms A, B, C, D, E, and F of ibrutinib. Is that correct?

20 "Answer: I believe that to be the case, yes.

21 "Question: Who was the first person, to your
22 knowledge, to identify form A?

23 "Answer: What do you mean by identify?

24 "Question: Who was the first person to isolate
25 and then characterize the polymorphic form that is referred

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1 to in this patent as form A?

2 "Answer: My understanding is David Wirth was
3 the first person to generate form A. I cannot remember off
4 the top of my head how much characterization he was able to
5 do at the time at Ceres. Characterization would likely have
6 been done by SSCI.

7 "Question: Same question for form B."

8 MS. BHARKHDA: Your Honor, we just paused. It
9 sounds like somebody needs to mute their mike.

10 TRIAL TECH: I just muted Jonathan Teppin.

11 THE COURT: Okay.

12 "Question: Same question for form B. Who was
13 the first person who isolate and identify what is now
14 referred to as crystalline form B in the '753 patent?

15 "Answer: I believe that to be David Wirth as
16 well.

17 "Question: And the same question for
18 crystalline form C identified in the '753 patent?

19 "Answer: Also David Wirth.

20 "Question: What about crystalline form B?

21 "Answer: Pharmorphix.

22 "Question: Okay. What about crystalline form
23 E? Who first identified and isolated crystalline form E?

24 "Answer: That should be Pharmorphix as well.

25 "Question: And what about crystalline form F?

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1 "Answer: That one's me, actually.

2 "Question: When did you, to the best of your
3 recollection, first identify and isolate crystalline form F?

4 "Answer: I don't remember the exact date. I
5 could -- I could dig it.

6 "Question: Is it fair to say that it was before
7 the filing of the patent application?

8 "Answer: Yes. That's a fair assumption.

9 "Question: Are any of the crystalline forms A
10 through F solvates?

11 "Answer: Yes.

12 "Question: Which ones?

13 "Answer: D, E, F.

14 "Question: And then if you could turn to column
15 -- starting in column 63 of the '753 patent. Answer: 63?

16 "Question: Column 63, yes.

17 You see the examples start in column 63?

18 "Answer: I do.

19 "Question: And Example 1 starts in example 63
20 and continues all the way to column 65.

21 Do you see that?

22 "Answer: Yes.

23 "Question: And I will repeat my question for
24 you.

25 Is it fair to say that you performed the

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1 experiment listed in column 65 under form F?

2 "Answer: Yes, it is fair to say that.

3 "Question: Is it also fair to say that the
4 examples for form A, B, C, D, and E under Example 1 were
5 performed by the other people you previously identified as
6 first isolating and identifying those forms?

7 "Answer: So for form D and E, I believe those
8 were Pharmorfix experiments.

9 "Question: Okay.

10 "Answer: But I would have to go back in here to
11 confirm to say positively --

12 "Question: Okay.

13 "Answer -- but I believe that to be the case.

14 "Question: And I believe for form A, you
15 previously testified that for routes 1 and 2, it was
16 Pharmorfix; and for Route 3, you weren't entirely sure. Is
17 that correct?

18 "Answer: That is correct. That's still the
19 case.

20 "Question: Okay. And then what about forms B,
21 routes 1 and 2, and form C?

22 "Answer: I'm not sure who performed those
23 experiments.

24 "Question: Okay. With regard to form F, was
25 anyone other than you responsible for isolating and then

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1 identifying that crystalline form?

2 "Answer: So I produced I, and Pharmorfix
3 characterized it.

4 "Question: I believe you said that --
5 previously testified that SSCI is the entity who
6 characterized form A. Is that correct?

7 "Answer: They did an initial characterization
8 of form A, yes, prior to Pharmorphix.

9 "Question: Was Pharmorphix the first company to
10 characterize form B?

11 "Answer: No.

12 "Question: Who was the first company to
13 characterize form B?

14 "Answer: SSCI, to the best of my knowledge.

15 "Question: And what about form C? Which
16 company was the first company to characterize form C?

17 "Answer: SSCI, to the best of my knowledge.

18 "Question. And what about form D? Which
19 company was the first company to characterize form D?

20 "Answer: Pharmorphix.

21 "Question: And what about form E? Which
22 company was the first company to characterize form E?

23 "Answer: Pharmorphix.

24 "Question: Mr. Goldman, I just have a few
25 questions for you.

1 Of the current employees at Pharmacyclics, who
2 is the person who is most knowledgeable about the
3 development of the crystalline form of ibrutinib?

4 "Answer: Likely myself.

5 "Question: And with regard to the work that
6 Pharmorphix did with respect to crystalline forms of
7 ibrutinib, who supervised that work?

8 "Answer: Myself and Dr. Smyth.

9 (End of videotaped deposition.)

10 MS. BHARKHDA: And, Your Honor, I'm going to let
11 my colleague, Mr. Abhyankar here, talk about the next
12 deposition we intend to introduce.

13 THE COURT: Okay.

14 MR. ABHYANKAR: Thank you, Your Honor. And if
15 plaintiffs don't have an objection, we're going to go a
16 little out of order than what we had presented to them based
17 on the time we have left, which I believe we only have about
18 15 minutes left, and play the testimony from Janet Dailey,
19 plaintiffs' prosecuting attorney. It's only 11 minutes
20 total.

21 THE COURT: Okay.

22 MR. ABHYANKAR: Thanks. Ms. Dailey was deposed
23 by defendants on December 10th, 2019. You will hear
24 11 minutes and 33 seconds of her deposition testimony, nine
25 minutes and 11 seconds for defendants and two minutes and

1 22 seconds for plaintiffs.

2 THE COURT: All right.

3 MS. BHARKHDA: Your Honor, I'm sorry. I was on
4 the other side of the room, so I apologize. It took me a
5 moment to get over here.

6 THE COURT: No problem.

7 MS. BHARKHDA: I think we do have one request
8 with respect to the testimony that's being played. You may
9 recall this was -- we would ask if we could for the
10 courtroom to be sealed or for the Court to be able to watch
11 this testimony without the public. This is for the reason
12 that was raised by Mr. Sipes in his opening statement about
13 wanting to protect Ms. Dailey.

14 THE COURT: I mean, I'm confused by this. This
15 person is employed by one of the defendants who is seeking
16 to play the testimony. Right?

17 MR. ABHYANKAR: Your Honor, to be clear, she was
18 Pharmacyclics' prosecuting attorney at the time of his
19 deposition of the relevant time frame.

20 She is currently --

21 THE COURT: Right. I'm saying she's currently
22 an employee of one of the defendants. Right?

23 MR. ABHYANKAR: Of one of the defendant's parent
24 companies, yes.

25 THE COURT: Ms. Bharkhda, I mean I don't

1 understand. In terms of protecting her reputational
2 interest, because that's what we're talking about, you would
3 think that, for all I know, she'll have a cause of action
4 against the defendant if it's as bad as you say. I just
5 don't really understand.

6 Do you understand? I mean --

7 MS. BHARKHDA: Your Honor, if you -- you know,
8 we can, we can withdraw the request and let it be played,
9 but given, you know, we wanted to -- we were, we wanted to
10 raise the issue in the interests of protecting her.

11 THE COURT: Yes. And I mean, like, I don't
12 know, you know. I feel funny in a way about it because I
13 like to protect people who are just innocent bystanders,
14 but she's affiliated with one of the parties and they want
15 to play it, so I'm going to overrule the objection. All
16 right.

17 I do have a notebook for it, so I can follow it.
18 Thank you. I take it back. I don't have a transcript. I
19 just have exhibits. You'll need to provide that is a well.
20 Thanks.

21 MR. ABHYANKAR: We will. Thank you.

22 (The videotaped deposition of Jana Dailey was
23 played as follows.)

24 "Question: Please state your name for the
25 record.

Dailey - deposition designations

1 "Answer: Jana Dailey.

2 "Question: Is that your full name?

3 "Answer: If you need a middle name, I can give
4 you a middle name. Jana Sook-Dailey.

5 "Question: Now, did you previously go by Jana
6 Lewis?

7 "Answer: Yes, that's correct.

8 "Question: And when did your name change over
9 from Jana Lewis to Jana Dailey?

10 "Answer: September 21st of this year, 2019.

11 "Question: Are you aware that Alvogen submitted
12 a paragraph IV notice letter relating to ibrutinib?

13 "Answer: Yes.

14 "Question: Have you seen the paragraph IV
15 notice -- Alvogen's paragraph IV notice letter?

16 "Answer: Yes.

17 "Question: Besides yourself, do you know if
18 anyone else at Foley has seen Alvogen's paragraph IV notice
19 letters?

20 "Answer: Yes.

21 "Question: Who?

22 "Answer: Hathaway Russell. And I'm not sure
23 about anyone else for that particular letter.

24 Question. Who sent you Alvogen's paragraph IV
25 notice letters?

Dailey - deposition designations

1 "Answer: I don't remember.

2 "Question: Is it someone at Foley?

3 "Answer: I don't remember.

4 "Question: Is it someone at Covington?

5 "Answer: I don't remember.

6 "Question: Is it someone at Janssen?

7 "Answer: I don't remember.

8 "Question: So you don't know what company or
9 law firm sent it to you?

10 "Answer: No, I don't remember which one it was.

11 "Question: Do you know why the paragraph IV
12 notice letter -- Alvogen's paragraph IV notice letter was
13 sent to you? Yes or no?

14 "Answer: Yes.

15 "Question: Why was Alvogen's paragraph IV
16 notice letter sent to you? I don't think I don't think I'm
17 going to instruct the witness not to answer that question on
18 the grounds that it would call for disclosure of attorney
19 client communications.

20 Q. Are you going to follow your counsel's objections?

21 A. Yes.

22 Q. Could you have answered that question if it weren't
23 for your counsel's objection and instruction?

24 "Answer: I think it might be privileged.

25 Question. But if it weren't privileged, you would be answer

Dailey - deposition designations

1 to answer:

2 Answer. Yes.

3 "Question: I've handed the witness a copy of
4 second preliminary amend under 37 C.F.R. Section 1.115
5 marked as Exhibit 16.

6 "Have you seen Exhibit 16 before?

7 "Answer: Yes.

8 "Question: When is the last time you've seen
9 Exhibit 16?

10 "Answer: I don't remember the last time I saw
11 this other than today.

12 "Question: Would you have seen it when you
13 prosecuted the '660 application?

14 Answer: Yes.

15 "Question: Do you know if you've seen this
16 exhibit after the patent issued?

17 "Answer: I don't remember.

18 "Question: Exhibit 16 is a preliminary
19 amendment submitted in connection with the 660 application
20 identified is on Exhibit 1. Correct:

21 "Answer: Yes.

22 "Question: And this was -- this amendment was
23 submitted on April 4, 2018?

24 "Answer: That's what the filing receipt and the
25 date says on the document.

Dailey - deposition designations

1 "Question: Exhibit 6 is a submission of an
2 amendment of claims; correct?

3 "Answer: Yes.

4 "Question: And Exhibit 16 -- 16 identifies new
5 claims that were submitted in connection with this 660
6 application, correct?

7 "Answer: Yes.

8 "Question: And those are identified on the
9 bottom of page 3 starting at claim 44 through 58, correct?

10 "Answer: So you're asking about the new claims?

11 "Question: Yes.

12 Answer: New claims, yes, 44 through 58 are
13 identified in the document.

14 "Question: Do you know who drafted the
15 claims -- the new claims of Exhibit 16?

16 "Answer: I don't know.

17 "Question: Do you know who would know?

18 "You can answer that yes or no if you know.

19 "Answer: Not for certain, no.

20 "Question: Are you aware that Sandoz has
21 submitted an ANDA for ibrutinib?

22 "Answer: Yes.

23 "Question: And are you aware of -- or do you
24 have any knowledge of the formulation of the ANDA product
25 described in Sandoz's ANDA?

Dailey - deposition designations

1 "Answer: Yes.

2 "Question: And how did you learn that?

3 "Answer: From the paragraph IV letter from
4 Sandoz.

5 "Question: And which paragraph IV letter?

6 "Answer: I don't remember the exact date, but
7 one from Sandoz to Pharmacyclics.

8 "Question: Have you ever drafted or amended a
9 claim in response to a paragraph IV notice letter?

10 "MR. YOUNKIN: Objection. I'm going to instruct
11 the witness not to answer. That calls for attorney/client
12 privileged communications.

13 "Question: Are you going to follow your
14 counsel's instruction:

15 "Answer: Yes.

16 "Question: And, of course, since we're asking
17 this question, and had there not been an instruction and
18 objection, would you have answered that question?

19 "Answer: Yes.

20 "Question: Exhibit 21 is entitled crystalline
21 form of Bruton's tie row sign kinase inhibitors. It's
22 marked with Bates number IMBPCYC04591386, and it continues
23 on the last page until 4591486.

24 "I'm going to direct your attention to the last
25 three pages of this document, starting on what's marked on

Dailey - deposition designations

1 the PDF as page 99 at the bottom, and the claims are at --
2 begin at the top of the page there.

3 "Are you there?

4 "Answer: Yes.

5 "Question: All of these claims required 2-Theta
6 angles -- claim 1 we're looking at.

7 "And claim 1 is describing a crystalline form A
8 of the chemical name for ibrutinib, that has an X-ray powder
9 diffraction XRPD pattern comprising 2-Theta peaks at 5.7
10 plus or minus 0.1 degrees, 18.9 plus or minus 01 degrees and
11 21.3 plus or minus 0.1 degrees.

12 "Do you see that?

13 "Answer: Yes, I see that.

14 "MR. BASS: Now I'm going to introduce the
15 amendment to this, which is -- I will introduce the second
16 preliminary amendment as the next exhibit, which is now --
17 that goes to you.

18 (Dailey Exhibit 22 was marked for
19 identification.)

20 "Question: This is the second preliminary
21 amendment under 37 C.F.R., Section 1.115.

22 Do you see that at the top on the first page
23 there?

24 "Answer: Yes.

25 "Question: Okay. I'm sorry. This bears the

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1 Bates number of IMBPCYC04591519, and this is for application
2 No. 15/900,660.

3 "Do you see that at the top in the caption
4 there?

5 "Answer: Yes.

6 "Question: Okay. Now, if you will flip to the
7 last page of this document -- or, no, excuse me -- if you
8 flip to where on the bottom it says 4591522, your signature
9 is on this document, correct?

10 "Answer: Yes.

11 "Question: Now, you'll see in the amendments to
12 the claim, which is on the next page, that claims 1 to 13
13 were canceled and that 14, which had been previously
14 presented, states -- because this is the second preliminary
15 amendment -- states, a crystalline form of the chemical name
16 for ibrutinib that has a differential scanning calorimetry
17 DSC thermogram having an endotherm with a peak of about 157
18 degrees Celcius.

19 "Do you see that?

20 "Answer: Yes, I do.

21 "Question: And you'll notice that it has a
22 crystalline form of and the chemical name for ibrutinib?

23 "Answer: Yes.

24 "Question. This is marked as IMBPCY0669461.

25 "Answer: Yes, I see that.

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1 "Question: Flip to the claims on the next
2 page. It says 101, 99, 100 on just the order it was
3 produced in.

4 "Do you recognize these claims?

5 "MR. YOUNKIN: That's a yes or no.

6 "Answer: I mean outside of today, I'm reminded
7 of these claims today, yes.

8 "Question: And what reminds you have these
9 claims today? Something I've introduced earlier?

10 "Answer: Yes.

11 "Question: What specifically?

12 "Answer: Exhibit 21.

13 (Dailey Exhibit 26 was marked for
14 identification.)

15 "Question: So this eventually became what is
16 U.S. patent No. 10, 294, '231, and this is the second
17 preliminary amendment under 37 C.F.R. to that patent.

18 Now --

19 "MR. YOUNKIN: The application -- okay.

20 "Question: -- if you flip over to this document
21 that I've just handed you, which is IMBPCYC0699612, you see
22 on the page on the bottom right that says -- ends in 618,
23 your signature is on that page, correct?

24 "Answer. Yes.

25 "Question: So that being said, if you look at

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1 the claims, they're not about a crystalline form of
2 ibrutinib any more, correct, in Exhibit 26?

3 "Answer: The claims are no longer about a
4 crystalline form.

5 "Question: Now, you see in 28, claim 14 (D) has
6 a limitation about 0.2 weight percent to about 1.0 weight
7 percent of lubricant.

8 "Do you see that?

9 "Answer: Yes.

10 "Question: And then you see on Exhibit 26,
11 14 -- claim 14 E is just lubricant. Do you see that?

12 "Answer: Yes, I see that the on page.

13 "Question: Now, you prosecuted both of these
14 patents, as I've asked you; correct?

15 "Answer: Yes.

16 "Question: Do you recall why one specifies the
17 concentration of lubricant and the other does not?

18 "Answer: No."

19 (End of videotaped deposition.)

20 THE COURT: Okay.

21 MR. ABHYANKAR: Your Honor, a little
22 housekeeping at the end of the day to introduce some
23 exhibits that were not introduced at the end of Dr. Steed's
24 examination.

25 THE COURT: Okay.

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1 MR. ABHYANKAR: As well as the exhibits from the
2 golden deposition clips and Ms. Dailey.

3 THE COURT: All right.

4 MR. ABHYANKAR: If I could proceed with that?

5 THE COURT: Yes.

6 MR. ABHYANKAR: For Dr. Steed we have DTX-1352,
7 JTX-322, JTX-1, DTX-2232, JTX-41, JTX-34, JTX-13, JTX-57,
8 JTX-68, JTX-56, DTX-07, DTX-1308, JTX-3, DTX-1304 and
9 DTX-2430.

10 THE COURT: All right. Any objection?

11 MR. SIPES: I believe that's missing one as
12 well. There's also JTX-506.

13 THE COURT: Okay.

14 MR. SIPES: And we probably should do PTX-14 owe
15 seven. That's the replacement for the one that was used
16 that's less confidential.

17 THE COURT: Okay.

18 MR. ABHYANKAR: Turning to Mr. Goldman's
19 testimony, we identified JTX-eight, DTX-66, JTX-557, DTX-68,
20 JTX-551, DTX-69 and DTX-73.

21 THE COURT: All right. Any objection? Wait.
22 Hold on. Any objection to those?

23 MR. SIPES: Your Honor, that was Goldman, I
24 think?

25 MR. ABHYANKAR: Right.

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1 THE COURT: We need the deposition transcripts
2 introduced, too. Right?

3 MR. ABHYANKAR: One second, Your Honor. We're
4 pulling those numbers.

5 THE COURT: Well, why don't we do this. Why
6 don't you all confer about it tonight and then come in
7 tomorrow morning and do this so that --

8 MR. ABHYANKAR: Okay.

9 THE COURT: It sounds like there were some joint
10 exhibits and I think it's probably best to coordinate on it.

11 Does that make sense?

12 MR. ABHYANKAR: Okay. Yes.

13 MR. SIPES: That makes sense, Your Honor.

14 THE COURT: All right.

15 MR. SIPES: We'll need to confer and we'll do
16 the same procedure for Dr. Swift's testimony because I think
17 we never got around to doing those as well.

18 THE COURT: Right. That would be good. All
19 right. Why don't you coordinate tonight. I think you tend
20 to jointly agree on these things.

21 MR. HANNA: That sounds good, Your Honor.

22 THE COURT: Anything else?

23 I said I would let Mr. Gutman respond later in
24 the day. I don't know if he still wanted to put anything on
25 the record. No?

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1 MR. HANNA: Right now there's nothing.

2 THE COURT: Okay. That sounds good. All right.

3 So then we're on for 8:30 tomorrow. Okay?

4 Anything else before the end of the day,
5 plaintiffs?

6 MR. SIPES: Nothing from plaintiffs, Your Honor.

7 THE COURT: Sandoz?

8 MR. ABHYANKAR: Nothing from Sandoz, Your Honor.

9 THE COURT: Alvogen?

10 MR. HANNA: Nothing for Alvogen.

11 THE COURT: Everybody have a good night.

12 MR. SIPES: Thank you.

13 (Court recessed at 6:00 p.m.)

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